Prevalence, recovery patterns and determinants of non-fatal outcome after trauma

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Publication date:
2020

Document Version
Publisher's PDF, also known as Version of record

Trauma is a leading cause of death and disability. Due to major improvements in trauma care in the past decades, the number of patients that survive their trauma has increased. However, worldwide, more than 1 billion trauma patients have to live with temporary or permanent disabilities, which can have a large impact on their life and which can lead to high medical and societal costs. Insights into non-fatal outcome following trauma and its determinants are vital in order to improve trauma care. The present thesis examined the prevalence, recovery patterns and determinants of non-fatal outcome for the hospitalized trauma population.

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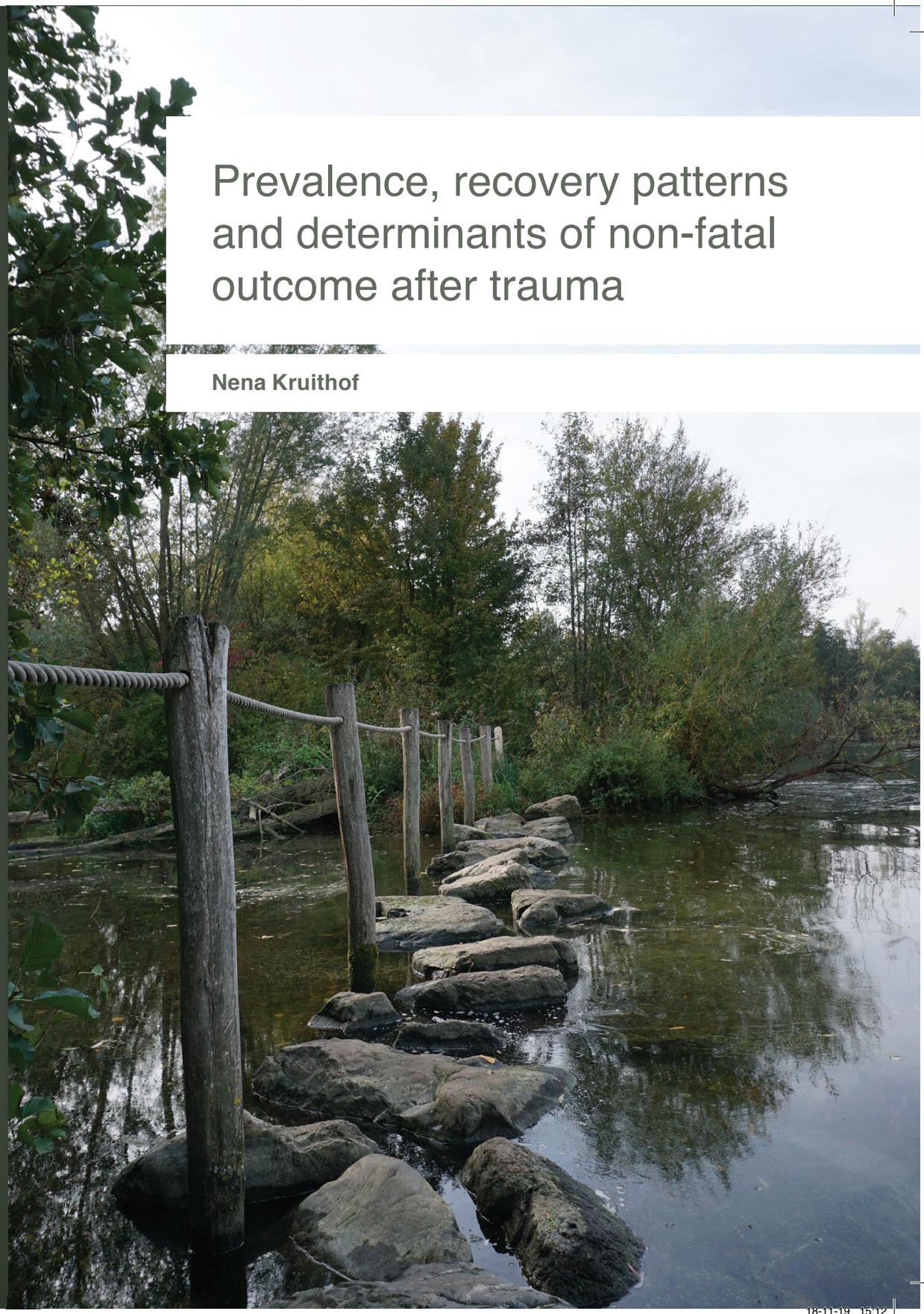

Prevalence, recovery patterns and determinants of non-fatal outcome after trauma

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Thesis, Tilburg University, the Netherlands

ISBN: 978-94-6375-565-8
Cover design: R.J.H. Martens
Graphic design & lay-out: Mafi Rad
Printing: Ridderprint

Prevalence, recovery patterns and determinants of non-fatal outcome after trauma

Proefschrift ter verkrijging van de graad van doctor aan Tilburg University
op gezag van Rector Magnificus, prof. dr. K. Sijtsma, in het openbaar te verdedigen ten overstaan van een door het college voor promoties aangewezen commissie in de Aula van de Universiteit op vrijdag 17 januari 2020 om 13.30 uur door

Nena Kruithof
geboren op 3 december 1990 te Woerden

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La qualité de la vie est plus importante que la vie elle-même

A. Carrel, chirurg, anatoom en bioloog (1873-1944)

Voor mijn ouders

CONTENTS

1

Chapter

General introduction and outline of the thesis

Trauma is a leading cause of death and disability (1-3). Due to major improvements in trauma care in the past decades, the number of patients that survive their trauma increased. Worldwide, more than 1 billion trauma patients have to live with temporary or permanent disabilities (1). A trauma can have a large impact on patients' life and can lead to high medical and societal costs (4-7). In the Netherlands, the in-hospital mortality rate of trauma patients is about 2% (8), indicating that 98% of the patients survive their trauma. Subsequently, there is a shift of attention from fatal towards non-fatal outcome after trauma.

Insights into non-fatal outcome following trauma and its determinants are vital in order to improve health care policy, to optimize prevention strategies and to develop effective health-care and rehabilitation services. This thesis aims to examine the prevalence, recovery patterns and determinants of non-fatal outcome for the hospitalized trauma population. This chapter presents several important topics related to the measurement of non-fatal outcome after trauma and addresses the research questions and outline of this thesis.

Trauma

There is a high diversity of external causes of trauma including road traffic injuries, drowning, poisoning, falls, burns or violence. Additionally, there is a large variety of injuries which can range from a single minor injury such as a contusion or a strain, to multiple severe injuries which includes for example severe bleedings or complex fractures in various body regions. Subsequently, trauma can be diverse, resulting in a considerable array of individual recovery patterns of non-fatal outcome.

Besides, there is a large variety of sociodemographic characteristics including age, gender and socio-economic status (SES) indicating the heterogeneity of the trauma population. As life expectancy is increasing, the number of elderly suffering from a trauma is rising as well (9-12). Under the age of 65, more males are admitted to the hospital after trauma while more females are admitted to the hospital from the age of 65 (8). Today, elderly females have the highest risk of becoming a trauma victim (1, 8).

The relative numbers of fatal and non-fatal trauma can be displayed in the form of a pyramid, i.e. the injury pyramid (**Figure 1**) (13, 14).

Figure 1: The injury pyramid (15)
Abbreviations: ICU, intensive care unit.

In the European Union (EU), most trauma patients are treated by a general practitioner without being referred to a hospital (16). However, trauma in the EU leads to 38 million visits to an emergency department (ED), 5 million hospital admissions and causes 200,000 deaths annually (17).

Trauma in the Netherlands

The sociodemographic and injury-related characteristics of the Dutch trauma population are comparable to trauma populations of other high-income countries. In the Netherlands, falls and road traffic accidents (mainly bicycle accidents) are the leading causes of trauma (8). About two-third of all Dutch patients seeks consultation by a general practitioner after their trauma (18). Yearly, around 700,000 trauma patients visit an ED in which 1 out of 6 patients is admitted to the hospital (19). Of these patients, 89% is admitted to a ward, 4% is admitted to an Intensive Care Unit, 3% needs acute surgery and 3% is referred to another hospital (8). The economic burden of trauma in the Netherlands is estimated €3,5 billion annually (4). Elderly females with a hip fracture as a result of a fall and males aged 18-65 with a road traffic accident show the highest economic burden due to the high medical care costs and high productivity losses, respectively (4).

Outcome after trauma

Until last decades, trauma research frequently relied on mortality rates (20) which is a hard endpoint. Nowadays, it becomes increasingly important to focus on non-fatal outcome since mortality rates decreased (1).

To increase comparability between studies and to assess the full impact of a trauma, Beeck et al. (21) developed a scientific guideline. The authors stated that trauma recovery consists of 4 phases including the acute treatment phase, the rehabilitation phase, the adaptation phase and the stable end situation. Trauma research should preferably cover each phase of recovery. Additionally, the authors recommend to retrospectively assess functioning prior to the trauma (21). To date, only a few studies adhered to this guideline (22-26).

In order to make an appropriate estimation of the impact of a trauma, a multidimensional approach is necessary which include data on a wide range of outcomes (27). Since a trauma has health consequences beyond the physical injury itself (28), non-fatal outcome should preferably be measured along three elements including health status (HS), Quality of Life (QoL) and psychological outcome. An integrated knowledge of these elements is vital to gain insight into the effects of a trauma, to identify risk groups of patients with worse outcome and to set priorities for prevention and to improve trauma care. However, several studies had been restricted either to HS (29-34), QoL (35, 36) or psychological outcome (37-40). Studies focussing on the multidimensional outcome for the entire trauma population are scarce. Therefore, there is still an ongoing need for measuring population-based data on the full spectrum of non-fatal outcome after trauma (27, 41). This thesis provides insight into the impact of a trauma on patients' life by examination of HS, QoL and psychological outcome.

Health status

Trauma differs widely with respect to disabilities. Some patients suffer from minor temporary disabilities while others suffer from severe long-life disabilities. HS assesses three domains including physical possibilities, state of mind and social activities. HS is generally measured with self-reported questionnaires in which patients indicate whether and to which extend they have problems on these domains (42).

Although disease specific measures are more sensitive to detect specific changes in health due to a certain condition or illness, they can not be used to make comparisons across different health domains. In contrast, generic measures are applicable to all diagnoses. Subsequently, generic measures are often used in trauma research since they are applicable to the large variety of ages, different trauma types and severity levels of the population.

To measure self-reported HS after trauma, the use of the EuroQol-five-dimension-3-level (43) and the Health Utilities Index Mark 2 and 3 (44), two generic measures, are recommended as common core of questionnaires (21). Both questionnaires generate a single summary score, i.e. a utility score. A utility score of 1 represents full health, 0 represents dead and negative values indicates a HS of worse than death (43, 44). HS can be used to quantify the difference between measured and perfect HS as well as quantifying a longitudinal change (45). Self-reported HS is an important outcome to determine non-fatal outcome since it quantify the impact of a trauma on population health over time. Moreover, HS enables comparison of 1) health outcome after trauma with other diseases, 2) HS prior to the trauma and 3) HS of the general population.

Quality of Life

Self-reported HS is determined without an evaluation or feeling about patient's own functioning (42). However, patients with the same clinical condition can report a different QoL (46). Therefore, QoL is an important and complementary outcome in health care research (47).

According to the World Health Organization (WHO), patients' satisfaction with functioning is the core of the definition of QoL (48). The Abbreviated World Health Organization Quality of Life Instrument (WHOQOL-BREF), an internationally applicable and generic instrument developed by the WHO (49), has been used in previous trauma studies to assess QoL (50-52). However, its methodological qualities in the trauma population are unknown. Therefore, examination of the methodological qualities of the WHOQOL-BREF for the trauma population is recommended to validly assess QoL after trauma.

Psychological outcome

Today, psychological functioning is recognised as an important outcome after trauma since a significant proportion of patients have a high risk to develop anxiety, depression or post-traumatic stress (53-58). Psychological problems after trauma can have a greater impact on QoL compared to the physical trauma itself (53, 59, 60). Besides, impairments of QoL can persist after resolution of the psychological symptoms (61). Furthermore, psychological problems after trauma play a crucial role in the development and maintenance of long-term disability (58, 62).

Methodological challenges

To make valid estimates of the impact of a trauma, epidemiological data on the incidence, severity and duration of the health consequences are essential (63). The large heterogeneity of the trauma population leads to methodological challenges. Important dilemmas include the variety of instruments to quantify the health impact of a trauma, the measurement of functioning prior to the trauma and obtaining outcomes in patients with temporary or permanent cognitive impairments. In the following paragraphs, each methodological challenge is described in more detail.

A variety of instruments and time assessments have been used to determine non-fatal outcome after trauma, which makes a comparison of the available disability estimates difficult. First, the heterogeneity of the trauma population is a major contributing factor to the incomparability of the methods (63). Second, previous studies focused on a variety of health domains (leading to incomplete information) at various moments in a variety of patient populations (leading to incomparable information) (21).

To produce valid estimates of the health impact and the decrease of functioning after trauma, information on patients' functioning prior to the trauma is crucial (64-67). Nevertheless, this information is often not available due to the difficulty to prospectively collect data soon after trauma (68). Subsequently, general population norms are often used as a proxy to indicate patients' functioning prior to the trauma (69-72). However, the trauma population is not a representative sample of the general population (68, 71, 73-76). For instance, as compared to the general population, the trauma population includes a higher percentage of people with a low SES (77, 78). SES in its turn is highly associated with HS (79).

Since not all patients are able to self-report their functioning, difficulties exist in obtaining outcomes for all patients. For that reason, it is recommend to make use of proxy assessments in trauma patients that are unable to complete the assessments themselves, e.g. in patients with severe dementia (21). However, previous studies often excluded patients with cognitive impairments or those with severe head injury (80-91). Though, exclusions based on characteristics related or not related to the trauma leads to selective patient samples that are not representative for the impact of a trauma at population level (21).

Aims and outline of this thesis

The aim of this thesis is to expand the knowledge on the prevalence, recovery patterns and determinants of non-fatal outcome after trauma. In addition to the review of the literature, the research as presented in this thesis was performed in all ten hospitals in the Noord-Brabant region, the Netherlands. The aim of this thesis was operationalized in the following research questions:

1. What is the course and what are the determinants of HS after trauma, what is the prevalence of psychological symptoms and what is the impact of a trauma on perceived QoL? (*Chapter 3 and 6*)
2. What is the effect of SES on non-fatal outcome after trauma? *(Chapter 4)*
3. Can educational level explain the difference in outcomes between retrospectively collected self-reported HS after trauma and self-reported HS of the general population? (*Chapter 5*)
4. Is the WHOQOL-BREF a valid and reliable questionnaire for the measurement of QoL in trauma patients? (*Chapter 7*)

Outline of this thesis

In *Chapter 2*, we describe the study protocol of the Brabant Injury Outcome Surveillance (BIOS), a large prospective cohort study focussing on non-fatal outcome after trauma. Results as presented in *Chapter 3, 5* and *7* in this thesis are derived from the BIOS.

In *Chapter 3*, we describe the course of self-reported HS and its determinants up until 2 year post-trauma. Besides, we report the prevalence rates of self-reported symptoms of anxiety, depression and post-traumatic stress.

In *Chapter 4,* we examine the measurements and interpretations of SES as a determinant of non-fatal outcome after trauma. In addition, we summarize the current knowledge of the effects of SES on non-fatal outcome.

In *Chapter 5*, we make a comparison between the self-reported retrospectively collected HS prior to the trauma and self-reported HS of a Dutch reference cohort. Hereby, we make adjustments for age, gender and especially educational level.

In *Chapter 6*, we aim to gain more insight into changes in perceived QoL after trauma by direct exploration of patients' point of view.

In *Chapter 7*, we examine the validity and reliability of the WHOQOL-BREF questionnaire for the hospitalized trauma population.

These parts are followed by the general discussion in *Chapter 8*. This chapter summarises the main findings of the included studies in this thesis, it answers the research questions and provides practical implications and recommendations for future research.

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2

Chapter

Prevalence, recovery patterns and predictors of quality of life and costs after non-fatal injury: the Brabant Injury Outcome Surveillance (BIOS) study

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Injury Prevention 2017;**23**:59
DOI:10.1136/injuryprev-2016-042032

ABSTRACT

Introduction: Trauma is a major public health problem worldwide that leads to high medical and societal costs. Overall, improved understanding of the full spectrum of the societal impact and burden of injury is needed. The main purpose of the Brabant Injury Outcome Surveillance (BIOS) study is to provide insight into prevalence, predictors and recovery patterns of short-term and long-term health-related quality of life (HRQoL) and costs after injury.

Methods: This is a prospective, observational, follow-up cohort study in which HRQoL, psychological, social and functional outcome and costs after trauma will be assessed during 24 months (mo) follow-up within injured patients admitted in 1 of 10 hospitals in the county Noord-Brabant, the Netherlands. Data will be collected by self-reported questionnaires at 1 week (including pre-injury assessment) and 1, 3, 6, 12 and 24mo after injury. If patients are not capable of filling out the questionnaires, proxies will be asked to participate. Also, information about mechanism and severity of injury, comorbidity and indirect and direct costs will be collected. Mixed models will be used to examine the course of HRQoL, functional and psychological outcome, costs over time and between different groups and to identify predictors for poor or good outcome.

Relevance: This study should make a substantial contribution to the international collaborative effort to assess the societal impact and burden of injuries more accurately. The BIOS results will also be used to develop an outcome prediction model for outcome evaluation including, besides the classic fatal, non-fatal outcome.

Trial registration number NCT02508675.

INTRODUCTION

Trauma is a major public health problem worldwide that remains one of the leading causes of death and disability and also leads to high medical and societal costs (1, 2).

Over the past decades, case fatality rates of severe injury have rapidly decreased, especially in countries with advanced health systems (3). This puts a growing number of patients at risk of serious long-term disability (4, 5). In other words, the burden of trauma has shifted largely from fatal to non-fatal outcome. Many of these patients with non-fatal injury are young people, whose daily activities like work and leisure may suffer greatly after trauma.

Improved understanding of the consequences of non-fatal injuries is needed for the evaluation of treatment approaches, to be able to guide policymakers in prioritising of injury prevention research, to facilitate the (economic) evaluation of interventions and to contribute to international efforts to more accurately assess the burden of non-fatal injuries. Although trauma is recognised as a leading cause of morbidity, there is worldwide a shortage of systematic and population-based injury follow-up data collection to inform understanding of the predictors and the multidimensional consequences of non-fatal injury (6, 7). Integrated knowledge of medical, physical, psychological, societal consequences and costs of injuries is scarce.

There is need for an improved understanding of injury outcomes, better identification of risk groups of poor outcomes and new insights into how disability following injury can be reduced (6). Up till now, there is insufficient systematic and population-based data collection and linkage to hospital data registries and trauma registries to fill this knowledge gap. Several prospective follow-up studies measuring the outcomes after trauma for a general injury population have been conducted nationwide and worldwide (8-15). However, only a few studies covered the wide range of outcomes. Traditionally, burden-of-injury studies have focused on a single outcome measure, for example, the physical consequences of injury, health-related quality of life (HRQoL) or return to work. Furthermore, only a few follow-up studies extend beyond 1 year after trauma (16), although residual disability at 1 year is often assumed to be perpetual. Besides this, most studies have been limited by small study size and substantial loss to follow-up.

Sound follow-up data on the incidence, severity and duration of the functional consequences and medical and societal costs of non-fatal injuries are needed. Data on all dimensions of functioning relevant to non-fatal injuries are needed to describe the pattern and risk factors of short-term and long-term outcome of injury patients over time. With the help of these data, the impact of injury on population health over time can be quantified.

Measuring the impact of injury is particularly challenging due to the large variation in injury types and severity. Therefore, it is important that valid methods will be used to estimate non-fatal injury outcome.

An important aspect is the choice of the study population. Although the association between severity of injury and long-term outcome is unclear (17), several studies included only specific injuries (18-20) or severely injured patients (4, 21-24). The definition of severe injury in these studies is mostly based on scores like the AIS and the ISS, which are correlated to survival chances and not to permanent disability after injury. To give a complete insight into the risk factors and recovery patterns of non-fatal injuries, a broad inclusion of injuries and severity levels is necessary.

Furthermore, it is important to measure a wide range of outcomes. Only a few follow-up studies measured psychological consequences such as post-traumatic stress disorder (PTSD) and depression. However, numerous studies have shown that psychological problems occur relatively frequently among trauma patients (17, 25-28).

Furthermore, comprehensive and detailed information on direct healthcare costs and productivity costs will help to identify injuries and high-risk groups. A small number of studies described the medical and societal costs (e.g. productivity loss) after injuries. However, costs enable rapid comparisons among very different types of injury. Intramural, extramural and societal costs can be high within the whole spectrum of injury patients.

In a former study, injury type, age, gender, length of hospital stay, intensive care unit (ICU) days, injury severity, post-traumatic stress symptoms and return to work were found to be associated with functional outcome and recovery (25, 26). Furthermore, important determinants of long-term disability after trauma are patients with one or more comorbidities (29), patients with multiple injuries (30) and frailty in elderly patients (31, 32).

Besides these known risk factors, we will also focus on social economic status and job-related factors. In earlier follow-up studies, the importance of (a combination of) these determinants remained often understudied. Most studies do not include all these risk factors simultaneously, which restricts the possibility to adjust for confounding accurately. However, measuring and investigating risk factors besides outcome offers the opportunity to develop a prediction model and risk profiles for non-fatal outcome.

A large part of the non-fatal injury patients are elderly. According to recent literature, frailty places a patient at risk for a poor outcome following even a minor illness or injury and it is predictive for patients' mortality, postoperative complications and discharge to skilled nursing facilities (31, 33). Besides that, a frail patient is vulnerable to develop geriatric syndromes and to experience functional decline already during hospitalisation (32).

Overall, improved understanding of the full spectrum of outcomes after injury is needed to better evaluate the predictors and recovery patterns after injury and to inform policymakers and guidelines to improve trauma care. Therefore, a population-based longitudinal survey of injured patients among the full spectrum of severity, including a large range of predictors and focusing on the multidimensional outcome after injury, is needed. This multidimensional approach is also needed to evaluate and improve the quality of trauma care.

Most outcome and performance evaluations of trauma care are classically based on mortality. However, the largest part of the trauma population survives. In the Netherlands, the mortality rate of the general acute hospitalised trauma population is 2% (34). Moreover, the prevalence of decreased functioning will be higher than the mortality rate.

Many different risk-adjusted models were developed in the past decades to predict mortality in trauma patients (35-38). A frequently used and cited model is the Trauma and Injury Severity Score (TRISS) (39). The TRISS is a logistic regression model of survival probability based on variables such as age, Revised Trauma Score (40) and ISS (41, 42). This model has been used in several countries.

In patients with traumatic brain injury (TBI), outcome models based on functional outcome and HRQoL have been established (36, 43, 44). As far as we know, models for non-fatal outcome on different aspects for a complete clinical trauma population have never been developed. Therefore, our study aims to develop a valid, reliable and accurate prediction model for developing risk profiles for non-fatal outcome after injury.

This paper describes the protocol of the Brabant Injury Outcome Surveillance (BIOS) study. The BIOS is a prospective longitudinal follow-up study among all admitted injury patients in the region Noord-Brabant independent of severity or classification of injury to evaluate the total non-fatal burden of injury from a patient and societal perspective.

The overarching purpose of the project is to provide a multidimensional overview of short-term and long-term prevalence of morbidity and recovery patterns after injury. Furthermore, this will result in improving and developing risk profiles in the trauma population. It will also create a base for measuring, comparing and improving quality of trauma care using non-fatal outcome.

OBJECTIVES

1. To investigate the short-term and long-term HRQoL, functional, psychological and economic outcome after non-fatal trauma;
2. To investigate the risk factors for decreased HRQoL, functional, psychological and economic outcome after non-fatal trauma;
3. To describe the healthcare use, medical costs and productivity loss due to non-fatal trauma;
4. To develop a risk profile for recovery after non-fatal injury in the short-term and long-term;
5. To validate and develop models for predicting non-fatal outcome after trauma;
6. To investigate whether a structural enlargement of the trauma registry with patient-reported outcome measurement does add value.

METHODS

Study design

The Brabant Trauma Registry (BTR) compiles prehospital and hospital data of all unintentional and intentional trauma patients admitted after presentation to the emergency department (ED) in 1 of 10 hospitals in the region Noord-Brabant (the Netherlands). The Dutch southern region Noord-Brabant has 2,4 million inhabitants and about 12 000 injured patients are admitted annually. The BTR includes 10 hospitals, 12 EDs and 1 Level 1 trauma centre. It covers representative amounts of urban and rural populations. As a result, the recorded injury incidence in the BTR is regarded as representative for the total population.

This is a prospective, observational, follow-up cohort study in which HRQoL, psychological and functional outcome and costs after trauma will be assessed during 24 months (mo) follow-up within injured patients admitted in 1 of the 10 hospitals of the BTR. The inclusion period will be 1 year; from 1 August 2015 until 31 July 2016. A flow diagram of the project is shown in **Figure 1**.

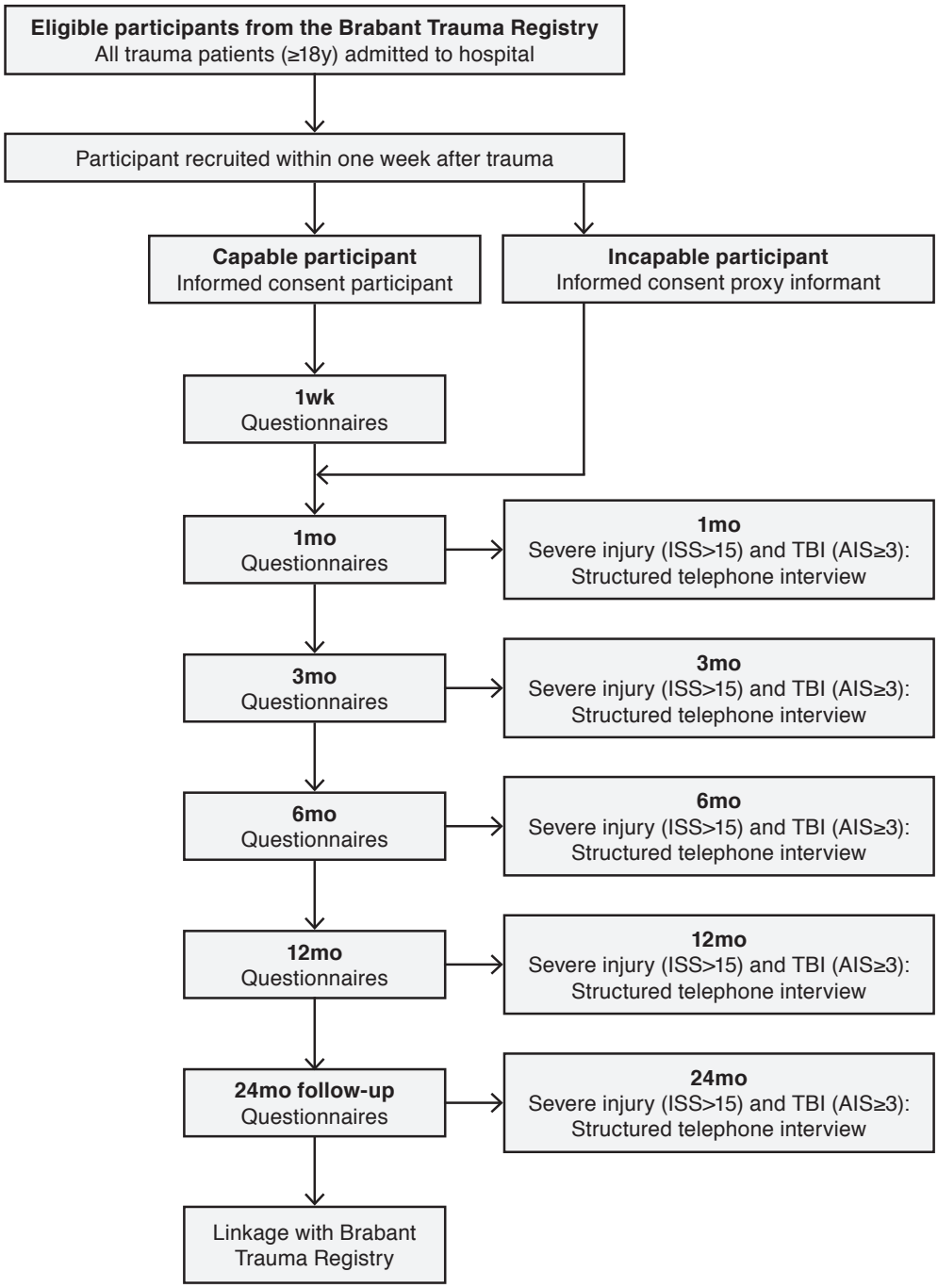

Figure 1: Flow diagram of the Brabant Injury Outcome Surveillance (BIOS) study
Abbreviations: wk, week; mo, month(s); ISS, Injury Severity Score; TBI, traumatic brain injury; AIS, Abbreviated Injury Scale.

Participants

Adult injury patients who are seen at the ED, who will be admitted to an ICU or a ward in Noord-Brabant and who survived to hospital discharge will be included in the study. Both intentional and unintentional injuries and all types and severity of injury will be included. A minimum age of 18 years and sufficient knowledge of the Dutch language are required. Patients with a pathological fracture caused by a malignancy or metastasis will be excluded.

In the region Noord-Brabant, there is no centre for the treatment of patients with severe burns. For that reason, patients with severe burns who are seen at the ED of a hospital in Noord-Brabant and who will be transferred to the nearest centre for patients with burns will be included as well.

If patients are incapable of completing the self-report measures themselves because of mental retardation, dementia or other neurological conditions, questionnaires will be completed by a proxy informant.

Data collection: registry data

Prehospital data (e.g. vital signs and transport modes), type of injury, diagnosis, injury severity and in-hospital medical procedures will be obtained directly from the BTR to provide a comprehensive description of the population.

Socio-demographic characteristics

Patient characteristics (e.g. age, gender, comorbidity, social economic status) will be electronically extracted from the BTR, Dutch Medical Registration and Electronic Medical Records and from the socio-demographic questions in the questionnaire.

Injury characteristics

Injury and admission data will be extracted from the BTR. The AIS (AIS-90, update 2008) (45, 46) is used to define the anatomical region and severity of separate injuries in detail and can be used to determine multiple injury. The ISS (41) is used to assess overall trauma severity. To compute the ISS, each of the six anatomical regions is scored with the highest AIS. The AIS values of the three most severely injured areas are squared and then summed. To reflect the physical reaction of the patient, the Glasgow Coma Scale, systolic blood pressure and respiratory rate are recorded at the moment the patient enters the ED. In addition, type (blunt or penetrating) and mechanism (e.g. traffic, fall) of trauma will be collected from the trauma registry.

Comorbidity

To measure comorbidities, we will use a modified version of the Cumulative Illness Rating Scale (CIRS) (47). The CIRS is a valid instrument to use in hospitalised patients. In addition, the measure was found to be an indicator of health status and demonstrated its ability to predict 18mo mortality and rehospitalisation in hospitalised elderly patients (48).

Data collection: follow-up questionnaires

Within the first week of hospital stay, patients will receive an information letter, informed consent form and the first questionnaire for the study either at the hospital or sent by post to patients home address. Patients will be asked if they prefer to fill in the questionnaires online or by paper and pencil in the future. Returned questionnaires do not contain names or other overt

identifiers, but are coded by number to link with the collected study data. Data will be collected by self-reported questionnaires at 1 week and 1, 3, 6, 12 and 24mo after injury. See **Table 1** for an overview of the measures and measure moments.

Table 1: Overview of the measures of the Brabant Injury Outcome Surveillance (BIOS)

Included patients			Measure points after injury							
			<1wk		1mo		3mo	6mo	12mo	24mo
			Pre-injury	Post-injury	Pre-injury	Post-injury				
Socio-demographic	All	Patient		x						
		Proxy				x				
Mod. CIRS	All	Patient		x					x*	
		Proxy				x			x*	
EQ-5D-3L	All	Patient	x	x		x	x	x	x	x
		Proxy			x	x	x	x	x	x
HUI2 Q3/ HUI3 Q6 (emotional wellbeing)	All	Patient	x							
		Proxy			x					
GFI	≥65yrs	Patient	x						x	
		Proxy			x				x	
HUI3 Q4 (use of walking aid)	≥65yrs	Patient	x						x	
		Proxy			x				x	
HUI2/ 3	All	Patient		x		x	x	x	x	x
		Proxy				x	x	x	x	x
HADS	All	Patient		x		x	x	x	x	x
		Proxy								
IES	All	Patient		x		x	x	x	x	x
		Proxy								
***i*MCQ**	All	Patient				x	x	x	x	x
		Proxy				x	x	x	x	x
***i*PCQ**	All	Patient				x	x	x	x	x
		Proxy				x	x	x	x	x
GOS-E	Severely injured (ISS>15) and/or TBI (AIS≥3)	Patient				x	x	x	x	x
		Proxy				x	x	x	x	x
QOLIBRI-OS	TBI (AIS≥3)	Patient				x	x	x	x	x
		Proxy				x	x	x	x	x

* only ≥ 65yrs

Abbreviations: wk, week; mo, month(s); Mod. CIRS, Modified Cumulative Illness Rating Scale; EQ–5D–3L, EuroQol–5D–3L; HUI, Health Utilities Index; GFI, Groningen Frailty Index; HADS, Hospital and Anxiety Depression Scale; IES, Impact Event Scale; iMCQ, iMTA Medical Consumption Questionnaire; iPCQ, iMTA Productivity Cost Questionnaire; GOS–E, Glasgow Outcome Scale Extended; ISS, Injury Severity Score: TBI, traumatic brain injury; AIS, Abbreviated Injury Scale; QOLIBRI–OS, Quality of Life after Brain Injury overall scale; yrs, years.

Proxy informants have to sign an informed consent form for proxies before participating in the study. Proxies will enrol in the study for the 1mo (2nd) questionnaire. They will receive a shorter and customised questionnaire since not all instruments can be filled out by proxy informants (see **Table 1**).

Severely injured patients (ISS>15) and patients with moderate-to-severe brain injury (AIS≥3) will receive a structured interview with the Glasgow Outcome Scale Extended (GOS-E) besides the standard set of questionnaires. In patients with brain injury (AIS≥3), the Quality of Life after Brain Injury overall scale (QOLIBRI-OS) will be administered as well. The structured interview will be performed during regular visits to the outpatient clinic or during consultation by telephone.

We will administer the following questionnaires:

- *EuroQol-5D-3L (EQ-5D-3L)* (49) to measure generic HRQoL. In the EQ-5D-3L, health is defined along five dimensions; mobility, self-care, usual activities, pain or discomfort and anxiety or depression. Each dimension has three levels: no problems, moderate problems or severe problems. A scoring algorithm is available by which each health status description can be expressed into a summary score. This summary score ranges from 0 for death and 1 for full health and can be interpreted as a judgement on the relative desirability of a health status compared with perfect health. The standard EQ-5D-3L classification does not include cognitive disability. Therefore, one item was added on cognition ("I have no/some/extreme problems with cognitive function, e.g. memory, concentration, coherence, IQ") (49). According to the review of Polinder *et al*. (16) the EQ-5D-3L has been used in various studies measuring HRQoL in trauma patients.

- *Health Utilities Index (HUI)* (50) to measure generic HRQoL. The HUI is a self-administered health status questionnaire that consists of 15 questions, which classifies respondents into either the HUI Mark 2 (HUI2) or the HUI Mark 3 (HUI3) health states. It covers the main health domains that are affected by injury, with particular focus on functional capacities. Results of the questionnaires are converted by an algorithm into the levels of the complementary HUI2 and HUI3 classification system to form seven-element and eight-element health state vectors. From these vectors, single-attribute and overall health state utility scores are calculated (50). The HUI2 and the HUI3 have been used in a large variety of clinical studies (51) and have been used in two recent studies (52, 53) in which trauma patients were involved. Furthermore, Polinder *et al.* (53) and Van Beeck *et al.* (54) stated that a combination of the EQ-5D-3L and the HUI should be used in trauma patients since the combination of both measures covers all relevant dimensions of health.

- *Hospital Anxiety and Depression Scale (HADS)* (55) is a self-reported 14-item questionnaire to screen for anxiety and depressive disorders. Both types of disorders are assessed with seven questions. The HADS has a four-point response scale (0–3) and subscale scores range from 0 to 21. Subscale values ≥11 for one of the subscales were regarded as a psychological complaint as this cut-off score provides the lowest proportion of false positives (1% for depression and 5% for anxiety) (55). In 2009, the HADS has been validated as a screening tool for depression and anxiety in patients with TBI (56). The HADS has been used in various studies including trauma patients (57-59).

- *Impact Event Scale (IES)* (60) to measure symptoms of PTSD. The IES is a 15-item self-report questionnaire that measures intrusive re-experiences of the trauma and avoidance of trauma-related stimuli (61). The respondent states whether the content of each statement was present using a four-point scale – 0 (not at all), 1 (rarely), 3 (sometimes) or 5 (often) – during the past seven days. The total score of the IES ranges from 0 to 75, a score of at least 35 represents the best cut-off for a probable diagnosis of PTSD (60). The IES has been widely used as a measure of stress reaction after a traumatic event and this questionnaire is able to discriminate between stress reactions at different times after the event. Furthermore, the IES has good convergent validity with observer-diagnosed PTSD (62). The IES has been used in earlier studies that included a population of trauma patients (58, 63).

- *iMTA Medical Consumption Questionnaire* (*i*MCQ) (64) is a recently developed non-disease-specific instrument for measuring (direct) medical costs. The *i*MCQ includes questions related to frequently occurring contacts with healthcare providers. The instrument is a standardised self-reported questionnaire and consists of 31 questions. The questions are based on the Dutch healthcare system. The *i*MCQ can be adapted for specific study populations and can be complemented with extra questions that are relevant for specific study populations (64-66).

- *iMTA Productivity Cost Questionnaire* (*i*PCQ) (67) is a recently developed non-disease-specific self-report questionnaire and is applicable to national and international studies. Currently, a Dutch and an English version of the *i*PCQ are available. The *i*PCQ includes 18 questions. As in the case of the *i*MCQ, the *i*PCQ can be adapted for specific study populations and can be complemented with extra questions that are relevant for specific study populations. Both indirect costs due to absenteeism as the productivity losses (i.e. presenteeism: sick, but working) are taken into account (67). The questions of the *i*PCQ are based on the Short–Form Health and Labour Questionnaire (SF-HLQ) (68), the PROductivity and DISease Questionnaire (69) and the QQ method (70). One question of the SF-HLQ will be added, a question about the cause(s) of reduced work capacity (e.g. concentration problems). Furthermore, two questions about pre-injury working status will be added. The *i*MCQ and the *i*PCQ have a similar structure and can be combined to measure productivity losses (direct and indirect costs) in detail (65, 67).

- *Glasgow Outcome Scale Extended (GOS-E)* (71) to measure functional outcome in patients with moderate-to-severe TBI (AIS≥3) and in severely injured patients (ISS>15). The GOS-E consists of eight questions covering consciousness, independence at home, major social roles (work, social and leisure activities, family and friendships) and return to normal life (33). It results in an eight-point scale classifying functional outcome from 1 (dead) to 8 (complete recovery). The GOS-E is a valid measure and is sensitive to change in patients with mild-to-moderate TBI (72). The GOS-E is frequently used to measure functional outcome in patients with TBI (73-77). Originally, the GOS-E was developed for measuring head injury outcomes. However, as it includes most domains from the World Health Organization (WHO) International Classification of Functioning, Disability and Health (78), the GOS-E is recommended for use in a trauma population. The GOS-E is considered a responsive measure in non-head-injured patients (79). To analyse the GOS-E outcomes of the severely injured patients, we will use the same dichotomised outcomes as stated in the

study of Gabbe *et al.* (30), a score of ≥7 represents 'good recovery', whereas a score <7 represents 'poor recovery'. GOS-E scores will be determined using a standard structured interview (71).

- *Quality of Life after Brain Injury overall scale (QOLIBRI-OS)* (80) to measure HRQoL in patients with moderate-to-severe TBI (AIS≥3). The QOLIBRI-OS is a recently developed measure and consists of six statements that cover areas including physical conditioning, cognition, emotions, function in daily life, personal and social life and current situation and future prospects. Response to each item will be scored 1 ('not at all') to 5 ('very'). The sum score of the QOLIBRI-OS can be converted arithmetically to a percentage scale; 0 represents the lowest possible HRQoL, whereas 100 represents the best possible HRQoL (80).The QOLIBRI-OS is a short version of the 37-item QOLIBRI scale and it assesses a similar construct to the QOLIBRI total score. The QOLIBRI-OS is considered a reliable and valid measure (81, 82).

- *Groningen Frailty Index (GFI)* (83) is a 15-item self-reported instrument to measure frailty. Frailty is defined as "a clinically recognizable state of increased vulnerability resulting from ageing-associated decline in reserve and function across multiple physiologic systems such that the ability to cope with every day or acute stressors is comprised" (84). Because we expect that frailty is a strong predictor in outcome after trauma, we will measure frailty in all patients aged 65 and older. The GFI screens for the loss of functions and resources in four domains of functioning: physical, cognitive, social and psychological (83, 85). The sum score of the GFI ranges from 0 to 15, with a score of ≥4 indicating frailty. The study of Peters *et al.* (86) concluded that the GFI is a feasible, reliable and valid self-assessment in home-dwelling and institutionalised elderly people.

Pre-injury and normative cohort data

Patients will be asked to fill in the EQ-5D-3L and two questions about emotional well-being of the HUI (HUI2 question 3 and HUI3 question 6) for the pre-injury status during the first 1 week questionnaire and proxy's during the second questionnaire (i.e. 1mo after injury). Patients 65 years and older will be asked to fill out one question of the HUI (HUI3 question 4) to determine patients' level of ambulation and the need of a walking aid pre-injury.

To examine differences in outcomes of the pre-injury health status of our study population compared with a comparable Dutch population, a reference cohort of 1,500 healthy individuals will be asked to fill out the same set of questionnaires as the included patients of our study measuring their pre-injury health status. We will make use of the data of the Longitudinal Internet Studies for the Social sciences (LISS) panel administered by CentERdata (Tilburg University, The Netherlands). It is known that adult hospitalised trauma patients are not a representative sample of the general population since the trauma study population differs regarding age, gender and socio-economic status (87-89). By using the LISS panel, we will adjust for these variables. The normative cohort data will be a useful tool, in which results can be compared with the BIOS results.

Healthcare consumption and costs

Costs will include direct intramural and extramural medical costs and indirect costs following absenteeism or presenteeism from work. The economic evaluation will be performed from a societal perspective in accordance with the Dutch guidelines (90).

Direct intramural medical costs due to treatment, complications and events during follow-up (e.g. ED visit, diagnostic work-up, therapy, surgery, admissions, follow-up visits) will be calculated. Real medical costs will be calculated by multiplying the volumes of healthcare consumption with the corresponding unit prices. All intramural activities registered after trauma will be obtained from the financial department of the hospital. We will use the unit prices determined by the financial department of the hospital, which are based on a detailed inventory and measurement of all resources used. For instance, the calculation of the costs of surgical procedures and hospital stay will consist of detailed measurement of investments in manpower, equipment, materials, housing and overhead.

Data on patients' extramural medical costs will be collected 1, 3, 6, 12 and 24mo post-injury by using the *i*MCQ. Last, indirect costs due to productivity loss will be calculated based on information on work absence and return to work. Information will be collected 1, 3, 6, 12 and 24mo using the *i*PCQ. Different methods exist to value productivity. The well-known human-capital method takes the patient's perspective and counts any hour not worked as an hour lost (91). By applying wage costs, the results of the *i*PCQ can be monetised and as such used in health economic evaluations.

Response rate

We will use some practical approaches to maximise the response rate. First of all, we will use prepaid reply envelopes. Second, all patients will be contacted by telephone by the research employees within 1 week after trauma on behalf of the participating hospitals. Third, patients can choose to fill in the questionnaires electronically or by paper and pencil. If necessary, we will send reminders with second copies of the questionnaires. Fourth, patients can still flow in into the study at 1 or 3mo after trauma.

In the BIOS study, we will investigate the injuries of a representative part of the Netherlands. Of all patients included in the Dutch Trauma Registry, 16% is admitted to 1 of the 10 hospitals of the region Noord-Brabant (34).

About 12,000 trauma patients are admitted in the Brabant region annually. Assuming 2,000 patients do not meet the inclusion criteria (deceased in hospital or aged <18), 10,000 patients can be recruited for the study.

Data analysis

All analyses will be conducted using Statistical Package for Social Sciences (SPSS) V.19.0.

Frequencies and descriptive statistics will be calculated to provide an overview of the characteristics of the study population. Statistical test results will be considered significant at a level of $p<0.05$. Student's t-test and one-way analysis of variance will be used to compare continuous variables. χ^2-tests will be performed for nominal variables. Mixed models will be used to examine the course of HRQoL, functional, psychological and societal outcome over time and between different groups. Missing values will be imputed according to the guidelines of the questionnaires. Socio-demographic, psychological and injury-related characteristics will be tested as risk factors of decreased HRQoL, functional, psychological and societal outcome and increased costs measured 1, 3, 6, 12 and 24mo after injury in simple and multiple regression analysis. Regarding the work ability after trauma, we will conduct survival analyses. The results of the proxy informants will be analysed separately.

Prediction model

For the prediction model of non-fatal outcome, we will use the data collected in the prospective study. Correlation between the different non-fatal outcome measures will be calculated with Spearman's rho test. Predictors for non-fatal outcome are assessed using stepwise multiple regression models. The performance of the models will be assessed in terms of calibration and discrimination. The validity of the final model will be tested. The role and effect of multiple imputation will be investigated.

FUTURE PERSPECTIVE

The BIOS study with a relatively large sample size, measurement of pre-injury and short-term and long-term functional outcomes and a wide range of outcome measures should constitute a detailed and comprehensive study of non-fatal injuries of varying severity. The focus on non-fatal outcomes and morbidity is critical as the burden of disability on society substantially outweighs the burden of mortality. The methodological developments and data from this study should also make a substantial contribution to the international collaborative effort to assess the societal impact and burden of injuries more accurately.

In traditional evaluation studies, observed and expected mortality are compared to assess quality of care. Regarding the increased survival rates, other outcome models are required to assess and improve the quality of trauma care. In our opinion, these models have to include fatal outcome, non-fatal outcome measures and costs. Little is known about the interaction between the different outcome aspects. Furthermore, it is plausible that predictors and scores in non-fatal outcome models are different from the classical fatal outcome models. As far as we know, models for non-fatal outcome on different aspects for a complete clinical trauma population have never been developed. The BIOS study results will be used to build a new model including fatal and non-fatal outcome.

The BIOS study will be a building block model with a base data set and opportunities to enlarge with specific data or questionnaires for specific injuries. For example, patients with a hip fracture and aged ≥65 are receiving extra questionnaires specific for quality of life within the elderly and functioning and pain after a hip fracture. Another example, patients with an acetabular fracture will be asked to complete the modified Merle d'Aubigne hip score (92) together with a medical expert during a standard visit to the outpatient clinic, next to the BIOS questionnaire. Furthermore, patients with a pelvic fracture will also be asked to complete the Majeed pelvic score (93).

One of the aims of this project is to investigate whether an enlargement of the trauma registry with patient-reported outcome measurement does add value. A part of this aim will be to define which questionnaires and data should be collected structurally.

The findings of the proposed BIOS study will have significant benefits for understanding the impact of non-fatal injury on personal and population health. This consistently collected empirical data will support the production of more valid burden-of-injury calculations, differences in outcomes and burden experienced by injury subgroups, cost-effectiveness analyses of injury prevention programmes and trauma care and support continuous quality improvement of care.

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3

Chapter

Health status and psychological outcome after trauma; a prospective multicenter cohort study

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ABSTRACT

Introduction: Survival after trauma has considerably improved. This warrants research on non-fatal outcome. We aimed to describe recovery patterns of health status (HS) and psychological outcomes during 24 months of follow-up and to identify subgroups at risk of both short and long-term health problems after trauma.

Methods: Hospitalized patients with all types of injuries were included. Data were collected at 1 week, 1, 3, 6, 12, and 24 months post-trauma. HS was assessed with the EuroQol-5D-3L (EQ-5D-3L) and the Health Utilities Index Mark 2 and 3 (HUI2/3). For the screening of post-traumatic stress, symptoms of anxiety and depression, the Impact of Event Scale (IES) and the Hospital Anxiety and Depression Scale (HADS) subscale anxiety (HADSA) and subscale depression (HADSD)) were used. Recovery patterns of HS and psychological outcomes were examined with linear mixed models analyses.

Results: A total of 4,883 patients participated (median age 68 (IQR 53-80); 50% response rate). The mean (SD) pre-injury EQ-5D-3L score was 0.85 (0.23). One week post-trauma, mean (SD) EQ-5D-3L, HUI2 and HUI3 scores were 0.49 (0.32), 0.61 (0.22) and 0.38 (0.31), respectively. These scores significantly improved to 0.77 (0.26), 0.77 (0.21) and 0.62 (0.35), respectively, at 24 months. Most recovery occurred up until 3 months. At long-term, higher age, comorbidities, longer hospital stay, lower extremity fracture and spine injury showed lower HS. The mean (SD) scores of the IES, HADSA and HADSD were respectively 14.80 (15.80), 4.92 (3.98), 5.00 (4.28) at 1 week post-trauma and slightly improved during 24 months post-trauma to 10.35 (14.72), 4.31 (3.76) and 3.62 (3.87), respectively.

Discussion: HS and psychological symptoms improved over time in which most improvements occurred within 3 months post-trauma. The effect of severity and type of injury faded out over time. At both the short-term and long-term, patients frequently reported symptoms of post-traumatic stress.

Trail registration: ClinicalTrials.gov identifier: NCT02508675.

Keywords: injury, trauma, hospitalization, longitudinal cohort study, health status, psychological outcome, determinants, prognostic factors

INTRODUCTION

Trauma poses a large burden on public health (1). Reduction of trauma-related mortality in high-income countries (2) resulted in increased numbers of trauma survivors with long-term injury impact, including reduced health status (HS). Improved understanding of the quality of survival of patients is critically important for improving health care quality and in evaluating trauma care. Furthermore, it is important to understand short- and long-term recovery patterns of HS by injury patient characteristics and to identify predictors of outcome of seriously injured patients (3, 4).

Establishing recovery patterns in the short- and long-term requires longitudinal data (5). Non-fatal outcome after trauma can be assessed with an overall measure of HS. HS includes patient's physical functioning, state of mind and social activities (6). In general, trauma has a large impact on HS (7-11), but large variations between patients are observed (10, 11).

Psychological problems, for example anxiety, depression and post-traumatic stress are often reported among trauma patients (12-17) and are associated with worse HS (7, 15).

Using a multidimensional approach to measure outcome including HS and symptoms of depression, anxiety and post-traumatic stress will result in a comprehensive understanding of non-fatal outcome after trauma. In addition, to assess prognostic factors for a poor outcome, it is important to cover the entire spectrum of the trauma population without exclusion of particular patient groups (e.g. elderly). The number of longitudinal cohort studies that examine multiple non-fatal outcomes in a large sample with a broad inclusion of type and severity of injury is limited (11, 18-22). Besides most studies start measuring at least 3 months after trauma, resulting in little knowledge about the real short-term consequences (10, 23-26).

The overall aim of the Brabant Injury Outcome Surveillance (BIOS), a population based longitudinal study, is to provide more insight into recovery patterns and determinants of non-fatal outcome after trauma. The aims of this population based study are 1. to describe the 2 year recovery patterns of HS and psychological outcome for different categories of trauma patients and 2. to identify prognostic factors for decreased short, mid and long-term HS. This information is important for understanding the short- and long-term recovery patterns and for best informing provision of trauma care to injured patients with long-term disability.

METHODS

Study design and participants

Data was obtained from the Brabant Injury Outcome Surveillance (BIOS). The BIOS-study is a prospective observational cohort study in which HS and psychological outcomes were assessed in injured patients in the first 24 months after trauma. The methods of the BIOS have been described in detail in the published research protocol (27).

Recruitment occurred in all ten hospitals of the Noord-Brabant region (the Netherlands) from August 2015 up until November 2016. Adults (≥18 years) who visited an emergency department ≤48 hours after trauma were invited to participate. All types of injuries were included, regardless of the intent or severity. Patients who died between hospital discharge and the first week

post-trauma, non-Dutch speaking patients, patients with no permanent address or patients with a pathological fracture were excluded. A proxy informant (caregiver or family member) was asked to complete the self-administered questionnaires if patients were incapable of participating in the BIOS-study themselves. Proxy informants were invited to enrol in the study at 1 month post-trauma. Informal caregivers (e.g. family members) and paid caregivers (e.g. nurses) were allowed to function as proxy informant.

The study was approved by the Medical Ethics Committee Brabant (project number NL50258.028.14 and NW2016-09). Prior to participation, participants signed an informed consent form.

Data collection

Questionnaires were sent at 1 week, 1, 3, 6, 12 and 24 months after trauma. Based on participants preference, follow-up questionnaires were either completed by paper and pencil or digitally. The questionnaires collected data on general patient characteristics, comorbidities, self-reported HS (i.e. EuroQol-5D-3L (EQ-5D-3L) (28), the Health Utilities Index (HUI) Mark 2 and Mark 3 (29)), self-reported psychological functioning (i.e. Hospital Anxiety and Depression Scale (HADS) (30) and the Impact of Event Scale (IES) (31)). Proxy informants did not complete questionnaires regarding psychological outcome.

In order to increase the response rate, patients who did not complete a questionnaire up until 3 months post-trauma were asked to complete a short version of the BIOS-questionnaire at 3, 6, 12 and 24 months after trauma. In this short questionnaire, educational level, comorbidities, the EQ-5D-3L and the IES were included.This short questionnaire did not include proxy assessment.

Outcome measures

The EQ-5D and HUI are used in various studies measuring HS after trauma (7, 10, 23, 25, 32-37). Besides, the EQ-5D in trauma patients provides valid results when this questionnaire is completed by a proxy informant (38). Moreover, a combination of the EQ-5D and the HUI were recommended to be used in trauma patients since the combination of these measures covers all relevant dimensions of health (35, 39).

The EQ-5D consists of the EQ-5D descriptive system and the EQ-visual analogue scale (EQ-VAS). The EQ-5D compressed the following five dimensions: ‘mobility’, ‘self-care’, ‘usual activities’, ‘pain/discomfort’ and ‘anxiety/depression’. Each dimension can be scored as ‘no problems’, ‘moderate problems’ or ‘severe problems’ (28). A summary score of these five dimensions (EQ-5D utility) can be calculated by using the Dutch tariffs (40). The EQ-VAS is a vertical visual analogue scale with 0 indicating the worst imaginable health state and 100 indicating the best imaginable health state. The EQ-5D and EQ-VAS were also measured pre-injury, by asking participants at 1 week or 1 month and proxy informants at 1 month for the patients’ health status before sustaining the injury. The EQ-VAS was not included in the short questionnaire.

The HUI is a self-administered HS questionnaire consisting of 15 questions, classifying respondents into either the HUI2 or HUI3 health states (29). Single-attribute and overall HS utility scores are calculated using the respective HUI2 and HUI3 utility functions (29).

For both the EQ-5D and the HUI, a scoring algorithm is used in which a score of 1 represents full health, 0 represents dead and negative values indicates a HS of worse than death (28, 29).

The Hospital Anxiety and Depression Scale (HADS) was used to assess symptoms of anxiety and depression (30). The HADS consists of 14 questions, 7 for symptoms of anxiety (HADSA) and 7 for depressive symptoms (HADSD). All questions have a 4-point response scale and the scores for both subscales ranged from 0 to 21. A higher subscale score indicates greater severity of symptoms for anxiety and depression with a subscale value of ≥11 indicating a probable case (30).

The IES was used to assess symptoms of post-traumatic stress (31). The IES consists of 15 items of which the patient could use a 4-point scale (0=not at all, 1=rarely, 3=sometimes and 5=often) whether the statement is present during the last seven days. A total sum score for the IES could be calculated ranging from 0 to 75. A sum score of ≥35 was considered as having symptoms of post-traumatic stress (31).

Prognostic factors

Hospital length of stay (LOS), admission to an Intensive Care Unit (ICU) and type and severity of injury were collected from the Brabant Trauma Registry and merged with the BIOS-data. The Abbreviated Injury Scale (AIS) codes (AIS-90, update 2008) (41) were used to create 14 injury group classifications (e.g. hip fracture, severe abdominal injury) representing the most common types of injuries (see **Appendix 3.A**). Patients who suffer multiple injuries could be classified in one or more injury group classifications.

Trauma severity was based on the Injury Severity Score (ISS). The ISS is based on the square of the highest Abbreviated Injury Scales (AIS) of the three most severely injured body regions with a range of 1 to 75. An ISS of ≥16 is considered severely injured (41).

Educational level was categorized in three levels; low (primary education, preparatory secondary vocational education or without diploma), middle (university preparatory education, senior general secondary education or senior secondary vocational education and training), and high (academic degree or university of applied science).

Statistical analyses

Patients were included in the analyses if they completed a questionnaire on at least one time point. For the non-responders of the BIOS, we could not obtain educational level. Therefore in the non-responders analysis, status scores of 2014 were used as a proxy to indicate socio-economic status (SES). Status scores were based on the mean income, % of people with a low income, % of people with low educational level and % of unemployed people in the neighborhood. In 2014, the mean status score in the Netherlands was 0.28 (42). Responders and non-responders were compared on age, gender, status score, ISS, type of trauma, LOS and admission to an ICU using Mann-Whitney U tests and Chi-square tests (χ^2).

Means and standard deviations (SDs) of the EQ-5D-3L, HUI2, HUI3, HADSD, HADSA and IES summary scores were calculated and reported for the total BIOS population and for different subcategories.

Multiple imputation was conducted with the Multivariate Imputation by Chained Equations procedure (43) to handle missing baseline characteristics and missing sum scores of the questionnaires due to missing item scores (see **Appendix 3.B**). The dataset was imputed 15 times with 5 iterations. Sensitivity analysis was performed in which only complete cases were included to compare results with the imputed datasets. For the imputed data, percentages of missing sum scores ranged from 30.1% to 63.6%.

Score options of each dimension of the EQ-5D were dichotomized into 0='no problems' and 1='moderate problems'/'severe problems'.

Four linear mixed models (44) with a random intercept were performed to assess longitudinal association between prognostic factors and HS during 24 months after trauma, short-term (1 week and 1 month), mid-term (3 and 6 months) and long-term (12 and 24 months). HS was measured with the EQ-5D-3L summary score.

Results were considered statistically significant at a level of $p<0.05$. All analyses were conducted in SPSS V.24 (Statistical Package for Social Sciences, Chicago, Illinois, USA), except of the multiple imputation which was performed in R version 3.4.0 (The R Project for Statistical Computing).

RESULTS

BIOS cohort

During the inclusion period of the BIOS, a total of 10,227 patients was hospitalized because of a trauma in one of the participating study centers. Patients were excluded since they did not speak the Dutch language (n=194), had no permanent address (n=32), died during their hospital stay within the first week after trauma (n=219) or had other reasons (n=8) (e.g. living abroad). Thus, 9,774 patients were eligible for participation in the BIOS of whom 4,883 patients provided informed consent and were included (50% response rate). Of these 4,883 participants, 1,099 filled out the shortened questionnaires (see **Appendix 3.C**).

At 1 week, 1, 3, 6, 12 and 24 months, we collected data of 1,776, 2,971, 3,109, 3,418, 3,105 and 2,734 participants (36.4%, 60.8%, 63.7%, 69.9%, 63.6% and 56.0%, respectively, of the study population) (see **Appendix 3.C**). A total of 1,105 participants (22.6% of the study population) completed all BIOS questionnaires at each time point. In addition, data on pre-injury HS were obtained in 3,366 participants (69.0% of the study population).

Study population

The median age of the study population was 68 years (IQR 53-80) (**Table 1**). Responders had a median ISS of 5 (IQR 4-9) and a total of 358 responders (7.0%) were admitted to the ICU. A large part of the population reported comorbidities; 1,426 (29.2%), 849 (17.4%) and 733 (15.0%) participants had 1, 2 or ≥3 comorbidities, respectively. Mild TBI (27.1%) and hip fracture (25.9%) were the most common types of trauma of participants included in the BIOS. The majority of the participants (n=2,562, 52.5%) had low educational level. In addition, 1,267 participants (25.9%) had middle educational level and 885 participants (18.1%) had high educational level. A total of 407 participants (8% of the study population) were represented by a proxy informant.

Compared to the non-responders, participants were more severely injured, were more often admitted to the ICU and had a lower SES. Patients aged 18-44 and ≥85 years showed relatively low response rates (35%-40% and 39%, respectively). Patients with minor injuries (ISS 1-3) revealed a low response rate (46%), as well as patients with a hospital LOS of ≤2 or ≥15 days (46% and 45%, respectively).

Table 1: Characteristics of responders and non-responders of the Brabant Injury Outcome Surveillance.

Characteristics	Responders (n=4,883) %	Non-responders (n=4,891) %
Gender (male)	2,329 (47.7%)	2,407 (49.0%)
Median age (yrs)	68 (IQR 53–80)	70 (IQR 46–84)
18-24	217 (4.4%)	400 (8.2%)
25-44	516 (10.6%)	767 (15.7%)
45-64	1,364 (27.9%)	1,006 (20.6%)
65-74	963 (19.7%)	563 (11.5%)
75-84	1,102 (22.6%)	1,030 (21.1%)
≥85	721 (14.8%)	1,125 (23.0%)
Missing	0 (0.0%)	0 (0.0%)
Median SES status score	0.33 (IQR -0.24–0.84)	0.13 (IQR -0.36–0.73)
Missing	60 (1.2%)	68 (1.4%)
Median days hospital LOS	4 (IQR 2–8)	4 (IQR 2–8)
≤2	1,325 (27.1%)	1,528 (31.2%)
3-7	1,944 (39.8%)	1,642 (33.6%)
8-14	937 (19.2%)	911 (18.6%)
≥15	346 (7.1%)	421 (8.6%)
Missing	331 (6.8%)	389 (8.0%)
Type of injury		
Pelvic injury	293 (6.0%)	151 (3.1%)
Hip fracture	1,266 (25.9%)	1,099 (22.5%)
Tibia, complex foot or femur fracture	569 (11.7%)	505 (10.3%)
Shoulder and upper arm injury	473 (9.7%)	417 (8.5%)
Radius, ulna or hand fracture	308 (6.3%)	283 (5.8%)
Mild TBI	1,324 (27.1%)	1,443 (29.5%)
Serious TBI	126 (2.6%)	130 (2.7)
Severe TBI	77 (1.6%)	77 (1.6)
Facial fracture	249 (5.1%)	303 (6.2%)
Thoracic injury	198 (4.1%)	162 (3.3%)
Rib fracture	541 (11.1%)	398 (8.1%)
Mild abdominal injury	87 (1.8%)	89 (1.8%)
Severe abdominal injury	36 (0.7%)	30 (0.6%)
Spinal cord injury	27 (0.6%)	10 (0.2%)
Stable vertebral fracture or disc injury	301 (6.2%)	249 (5.1%)
Injury severity	5 (IQR 4–9)	5 (IQR 2–9)
1-3	1,145 (23.4%)	1,360 (27.8%)
4-8	1,597 (32.7%)	1,320 (27.0%)
9-15	1,857 (38.0%)	1,627 (33.3%)
≥16	239 (4.9%)	194 (4.0%)
Missing	45 (0.9%)	390 (8.0%)

Table 1 *(continued)*

Characteristics	Responders (n=4,883) %	Non-responders (n=4,891) %
ICU-admission (yes)	358 (7.3%)	292 (6.0%)
Missing	0 (0.0%)	0 (0.0%)

Abbreviations:SES, social–economic status; ICU, intensive care unit; ISS, Injury Severity Score; IQR, Interquartile range; LOS, length of stay; TBI, traumatic brain injury; yrs, years.

Health status

The mean EQ-5D-3L summary score increased from 0.49 (SD 0.32) at 1 week post-trauma to 0.56 (SD 0.30), 0.69 (SD 0.27), 0.74 (SD 0.25), 0.76 (SD 0.25) and 0.77 (SD 0.26) at 1, 3, 6, 12 and 24 months post-trauma, respectively. The mean pre-injury EQ-5D score was 0.85 (SD 0.23). In addition, mean (SD) HUI2 and HUI3 scores increased from 0.61 (0.22) and 0.38 (0.31) at 1 week post-trauma to 0.77 (0.21) and 0.62 (0.35) at 24 months post-trauma, respectively (see **Table 2**). With regard to the individual domains of the EQ-5D, trauma patients reported most problems on the 'mobility, 'usual activities' and 'pain/discomfort' dimensions during 24 months of follow-up (see Fig 1). In addition during 24 months, the prevalence of problems on all dimensions of the EQ-5D decreased, but remained higher at 24 months compared to pre-injury (46% and 32%, respectively for mobility, 23% and 16%, respectively for self-care, 44% and 26%, respectively for usual activities, 52% and 32%, respectively for pain/discomfort and 22% and 16%, respectively for anxiety/depression).

Table 2: Mean (SD) summary scores of self-reported health status and psychological outcomes up until 2 year post-trauma.

Time post-trauma	EQ-5D-3L*	HUI2**	HUI3**	HADSA***	HADSD***	IES****
1 week	0.49 (0.32)	0.61 (0.22)	0.38 (0.31)	4.92 (3.98)	5.00 (4.28)	14.80 (15.80)
1 month	0.56 (0.30)	0.67 (0.22)	0.45 (0.35)	4.81 (3.95)	4.77 (4.17)	14.44 (15.73)
3 months	0.69 (0.27)	0.72 (0.22)	0.53 (0.35)	4.57 (3.80)	4.24 (4.02)	12.75 (15.47)
6 months	0.74 (0.25)	0.75 (0.22)	0.58 (0.35)	4.21 (3.79)	3.91 (4.01)	11.42 (15.28)
12 months	0.76 (0.25)	0.76 (0.22)	0.60 (0.36)	4.32 (3.78)	3.74 (3.97)	10.98 (14.98)
24 months	0.77 (0.26)	0.77 (0.21)	0.62 (0.35)	4.31 (3.76)	3.62 (3.87)	10.35 (14.72)

*Completed by total study population. **Not administered in patients who completed only the short questionnaire.
***Not administered in proxy participants, and in patients who completed only the short questionnaire.
****Not administered in patients aged ≥65 with a hip fracture who completed only the short questionnaire.
Abbreviations: SD, standard deviation; EQ–5D–3L, EuroQol–5D–3L; HUI2/3, Health Utilities Index Mark 2/3; HADS, Hospital Anxiety and Depression Scale; HADSA, Hospital Anxiety and Depression scale, subscale anxiety; HADSD, Hospital Anxiety and Depression scale, subscale depression; IES, Impact of Event Scale.

Psychological outcomes

The mean summary scores (SD) of the HADSA (symptoms of anxiety), HADSD (symptoms of depression) and IES (symptoms of post-traumatic stress) slightly decreased from 4.92 (3.98), 5.00 (4.28) and 14.80 (15.80), respectively, at 1 week post-trauma to 4.31 (3.76), 3.62 (3.87) and 10.35 (14.72), respectively, at 24 months post-trauma (see **Table 2**).

Prevalence rates of symptoms of anxiety (HADSA≥11), depression (HADSD≥11) and post-traumatic stress (IES≥35) reported at 1 week post-trauma were 10.2%, 12.3% and 13.5%, respectively, and showed a small decrease over time to 7.7%, 7.5% and 10.3% at 12 months and 7.8%, 6.8% and 11.0% at 24 months post-trauma, respectively.

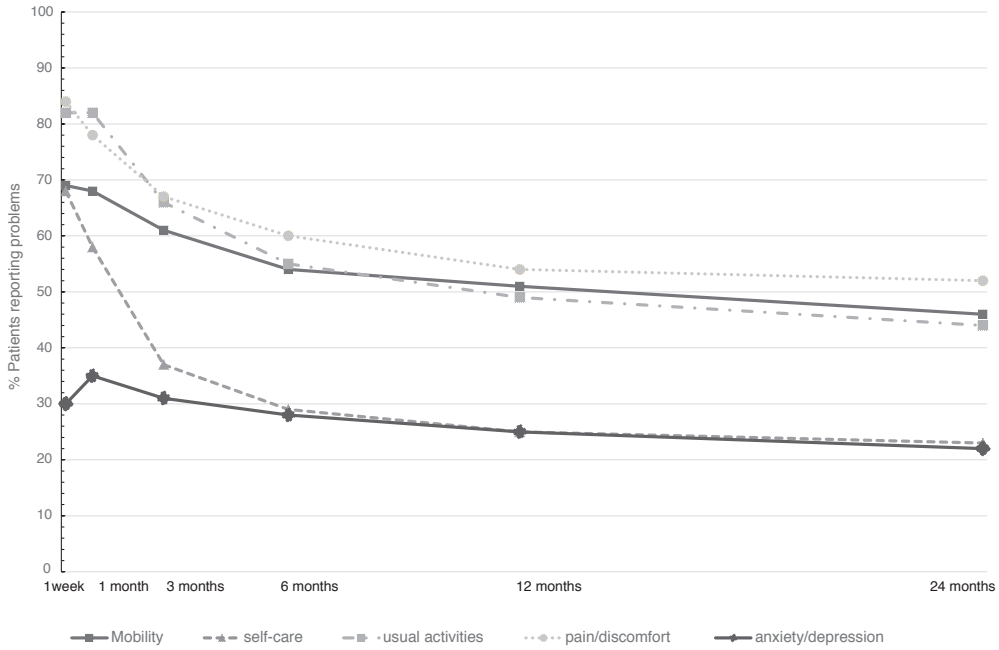

Figure 1: Prevalence of moderate or severe problems (%) on each EuroQol–5D–3L dimension up until 2 years of follow–up.

Prognostic factors of health status

Overall HS measured as with EQ-5D-3L increased up until 6 months for all groups of patients and stabilized between 6 and 12 months post-trauma for most groups (see **Table 3**). Female patients had a lower HS compared to males at every time point.

At all time points, patients aged 85 and older had the lowest HS compared to the other age categories (0.40; SD 0.33 at 1 week and 0.39; SD 0.32 at 24 months) At 3 and 6 months, all patient groups between 25 and 74 years reported the same HS whereas patients aged between 18 and 24 reported a higher EQ-5D summary score. HS stabilized at 6 or 12 months for every age group, except for patients between 25 and 44 years for whom HS increased further.

Except for 1 week, at all time points patients with a high educational level had the highest HS. With increasing number of comorbidities, HS decreased. Patients with 3 or more comorbidities had an EQ-5D-3L summary score from 0.40 (SD 0.33) at 1 week to 0.59 (SD 0.29) at 12 and 24 months after trauma. Patients with moderate injuries (ISS 9-15) showed on almost each time point the lowest HS and ended up with a EQ-5D-3L summary score of 0.72 (SD 0.28) at 24 months after trauma. At 1 week, severely injured patients (ISS ≥ 16) showed the lowest mean HS (0.28 SD 0.35).

Patients with the longest hospital stay (≥ 15 days) had the lowest mean HS at all time points, ranging from 0.28 (SD 0.34) at 1 week up to 0.62 (SD 0.28) at 24 months after trauma.

Table 3: Self-reported health status for patient and injury characteristics as measured with the EuroQol-5D-3L.

Characteristics		Mean (SD) EQ-5D-3L summary score					
		1 week	1 month	3 months	6 months	12 months	24 months
Gender	**Male**	0.54 (0.32)	0.62 (0.28)	0.74 (0.25)	0.79 (0.23)	0.83 (0.21)	0.84 (0.21)
	Female	0.43 (0.31)	0.50 (0.30)	0.64 (0.28)	0.69 (0.26)	0.70 (0.27)	0.72 (0.28)
Age (yrs)	**18-24**	0.50 (0.32)	0.63 (0.24)	0.79 (0.24)	0.85 (0.21)	0.86 (0.21)	0.86 (0.22)
	25-44	0.45 (0.30)	0.59 (0.29)	0.74 (0.24)	0.79 (0.24)	0.84 (0.22)	0.87 (0.19)
	45-64	0.49 (0.31)	0.60 (0.27)	0.73 (0.24)	0.79 (0.21)	0.83 (0.21)	0.83 (0.22)
	65-74	0.51 (0.31)	0.62 (0.28)	0.73 (0.24)	0.79 (0.22)	0.80 (0.22)	0.81 (0.23)
	75-84	0.52 (0.33)	0.53 (0.31)	0.66 (0.27)	0.70 (0.25)	0.70 (0.26)	0.70 (0.28)
	≥85	0.40 (0.33)	0.39 (0.32)	0.50 (0.29)	0.55 (0.29)	0.57 (0.29)	0.56 (0.30)
Educational level	**Low**	0.49 (0.33)	0.52 (0.31)	0.65 (0.28)	0.70 (0.27)	0.71 (0.27)	0.72 (0.28)
	Middle	0.50 (0.31)	0.59 (0.29)	0.71 (0.26)	0.77 (0.24)	0.80 (0.23)	0.81 (0.23)
	High	0.48 (0.30)	0.62 (0.26)	0.75 (0.23)	0.80 (0.21)	0.84 (0.20)	0.86 (0.20)
Comorbidity	**0**	0.53 (0.30)	0.65 (0.26)	0.77 (0.23)	0.83 (0.19)	0.86 (0.18)	0.87 (0.18)
	1	0.49 (0.32)	0.56 (0.29)	0.69 (0.25)	0.75 (0.24)	0.77 (0.24)	0.78 (0.25)
	2	0.45 (0.30)	0.47 (0.31)	0.61 (0.29)	0.66 (0.26)	0.67 (0.27)	0.68 (0.28)
	≥3	0.40 (0.33)	0.42 (0.32)	0.56 (0.29)	0.58 (0.29)	0.59 (0.29)	0.59 (0.29)
ISS	**1-3**	0.63 (0.29)	0.69 (0.27)	0.78 (0.23)	0.79 (0.24)	0.79 (0.25)	0.81 (0.25)
	4-8	0.46 (0.31)	0.56 (0.29)	0.71 (0.25)	0.77 (0.23)	0.80 (0.22)	0.81 (0.23)
	9-15	0.43 (0.30)	0.50 (0.30)	0.63 (0.28)	0.68 (0.27)	0.70 (0.28)	0.72 (0.28)
	≥16	0.37 (0.35)	0.50 (0.31)	0.65 (0.30)	0.74 (0.25)	0.77 (0.24)	0.77 (0.25)
LOS (days)	**≤2**	0.61 (0.29)	0.70 (0.25)	0.81 (0.21)	0.83 (0.20)	0.84 (0.22)	0.86 (0.21)
	3-7	0.47 (0.30)	0.55 (0.28)	0.69 (0.25)	0.74 (0.24)	0.77 (0.24)	0.79 (0.24)
	8-14	0.31 (0.31)	0.46 (0.29)	0.59 (0.29)	0.65 (0.27)	0.68 (0.28)	0.67 (0.29)
	≥15	0.28 (0.34)	0.32 (0.31)	0.50 (0.29)	0.58 (0.28)	0.60 (0.28)	0.62 (0.28)

Abbreviations: SES, socio–economic status; SD, standard deviation; EQ–5D, EuroQol–5D–3L; ISS, Injury Severity Score; LOS, length of hospital stay; yrs, years.

Table 4 shows the results of the multivariable longitudinal analysis. After adjustment for confounding, short-term (1 week and 1 month) prognostic factors for a significant lower EQ-5D summary score were female gender, higher number of comorbidities, longer LOS, higher ISS, pelvic injury, tibia/complex foot or femur fracture, radius/ulna/hand fracture, shoulder/upper arm injury, rib fracture, spinal cord injury and stable vertebral fracture/disc injury. Mid-term (3 and 6 months) prognostic factors were higher number of comorbidities, ISS between 4 and 15, longer LOS, radius/ulna/hand fracture, tibia/complex foot or femur fracture, severe TBI, spinal cord injury and stable vertebral fracture/disc injury. At long-term (12 and 24 months) age 75 and above, 2 or more comorbidities, longer LOS, tibia/complex foot or femur fracture, spinal cord injury and stable vertebral fracture/disc injury were prognostic factors for lower HS. High educational level was associated with higher HS in the long-term analysis.

DISCUSSION

This study describes HS and psychological outcome and recovery patterns during 24 months after trauma. Besides, prognostic factors for lower HS were investigated. HS markedly improved during 24 months after trauma of which most recovery occurred within the first 3 months. Compared to pre-injury HS, a large decrease in HS was found at 1 week post-trauma.

Table 4: Longitudinal analysis of short, mid and long-term prognostic factors of decreased health status as measured with the EQ-5D-3L.

Characteristics		Total (1 week-24 months)	Short-term (1 week-1 month)	Mid-term (3-6 months)	Long-term (12-24 months)
		* Beta (95% CI)	* Beta (95% CI)	* Beta (95% CI)	* Beta (95% CI)
		n=4,809	n=3,314	n=4,048	n=3,422
Gender	Male	ref	ref	ref	ref
	Female	-0.05 (-0.06; -0.04)	-0.06 (-0.08; -0.05)	-0.05 (-0.06;-0.03)	-0.06 (-0.08; -0.05)
Age (yrs)	18-44	ref	ref	ref	ref
	45-64	0.04 (0.02; 0.05)	0.06 (0.04; 0.09)	0.02 (-0.00; 0.04)	0.01 (-0.01; 0.03)
	65-74	0.09 (0.08; 0.11)	0.14 (0.11; 0.17)	0.07 (0.05; 0.09)	0.04 (0.02; 0.06)
	≥75	0.02 (0.01; 0.04)	0.09 (0.06; 0.12)	-0.01 (-0.03; 0.01)	-0.05 (-0.07; -0.02)
Educational level	Low	ref	ref	ref	ref
	Middle	0.02 (0.00; 0.03)	0.01 (-0.01; 0.03)	0.01 (-0.00; 0.02)	0.03 (0.01; 0.04)
	High	0.03 (0.02; 0.05)	0.02 (-0,01; 0,04)	0.04 (0.02; 0.05)	0.05 (0.04; 0.07)
Number of comorbidities	None	ref	ref	ref	ref
	1	-0.06 (-0.07; -0.05)	-0.06 (-0.08; -0.04)	-0.06 (-0.07; -0.04)	-0.05 (-0.07; -0.04)
	≥2	-0.15 (-0.16; -0.14)	-0.14 (-0.17; -0.12)	-0.14 (-0.16;-0.13)	-0.16 (-0.18; -0.15)
ISS	1-3	ref	ref	ref	ref
	4-8	0.00 (-0.01; 0.02)	-0.03 (-0.06; -0.01)	0.01 (-0.05; 0.03)	0.03 (0.01; 0.05)
	9-15	-0.02 (-0.04; -0.00)	-0.06 (-0.09; -0.02)	-0.02 (-0.04; -0.01)	0.00 (-0.02; 0.03)
	≥16	0.01 (-0.01; 0.04)	-0.02 (-0.08; 0.04)	0.01 (-0.04; 0.05)	0.04 (-0.01; 0.08)
LOS	≤2	ref	ref	ref	ref
	3-7	-0.05 (-0.06; -0.04)	-0.08 (-0.10; -0.06)	-0.06 (-0.07; -0.04)	-0.03 (-0.04; -0.01)
	8-14	-0.11 (-0.12; -0.09)	-0.15 (-0.18; -0.12)	-0.11 (-0.13; -0.09)	-0.08 (-0.11; -0.06)
	≥15	-0.20 (-0.22; -0.18)	-0.24 (-0.28; -0.20)	-0.20 (-0.23; -0.17)	-0.17 (-0.20; -0.14)

Table 4 *(continued)*

Characteristics		Total (1 week-24 months)	Short-term (1 week-1 month)	Mid-term (3-6 months)	Long-term (12-24 months)
		* Beta (95% CI)	* Beta (95% CI)	* Beta (95% CI)	* Beta (95% CI)
		n=4,809	n=3,314	n=4,048	n=3,422
Injury	Pelvic injury	-0.05 (-0.07; -0.03)	-0.13 (-0.16; -0.10)	-0,01 (-0.04; 0.01)	0.00 (-0.02; 0.03)
	Hip fracture	-0.02 (-0.04; -0.01)	-0.02 (-0.05; 0.01)	-0.03 (-0.05; -0.00)	-0.02 (-0.05; 0.00)
	Tibia, complex foot or femur fracture	-0.05 (-0.06; -0.04)	-0.11 (-0.14; -0.08)	-0.05 (-0.07; -0.02)	-0.02 (-0.04; 0.00)
	Shoulder and upper arm injury	-0.03 (-0.04; -0.01)	-0.07 (-0.10; -0.05)	-0.02 (-0.04; 0.00)	-0.00 (-0.02; 0.02)
	Radius, ulna or hand fracture	0.00 (-0.02; 0.02)	-0.03 (-0.06; 0.00)	0.00 (-0.02; 0.03)	0.02 (-0.00; 0.05)
	Mild TBI (AIS 1-2)	0.03 (0.02; 0.04)	0.06 (0.04; 0.08)	0.03 (0.02; 0.05)	0.02 (-0.00; 0.03)
	Serious TBI (AIS 3)	0.04 (-0.01; 0.07)	0.07 (0.02; 0.13)	0.05 (0.01; 0.10)	0.01 (-0.03; 0.05)
	Severe TBI (≥ 4)	-0.03 (-0.06; 0.02)	-0.02 (-0.10; 0.07)	-0.06 (-0.12; 0.00)	-0.01 (-0.07; 0.05)
	Facial fracture	0.02 (0.01; 0.04)	0.05 (0.01; 0.09)	0.02 (-0.01; 0.04)	0.01 (-0.01; 0.04)
	Thoracic injury	0.04 (0.02; 0.06)	0.05 (0.01; 0.10)	0.04 (0.02; 0.07)	0.03 (-0.01; 0.06)
	Rib fracture	0.01 (-0.00; 0.03)	-0.01 (-0.04; 0.01)	0.03 (0.01; 0.05)	0.01 (-0.01; 0.04)
	Mild abdominal injury	0.02 (-0.02; 0.05)	0.04 (-0.02; 0.10)	0.01 (-0.04; 0.05)	0.02 (-0.03; 0.07)
	Severe abdominal injury	0.03 (-0.02; 0.08)	-0.05 (-0.15; 0.05)	0.06 (-0.04; 0.13)	0.05 (-0.02; 0.13)
	Spinal cord injury	-0.11 (-0.17; -0.05)	-0.10 (-0.22; 0.03)	-0.12 (-0.20; -0.03)	-0.15 (-0.23; -0.07)
	Stable vertebral fracture or disc injury	-0.05 (-0.07; -0.03)	-0.08 (-0.12; -0.05)	-0.05 (-0.08; -0.03)	-0.03 (-0.06; -0.01)

** Mixed Models, adjusted for all other variables*

Abbreviations: ISS, Injury Severity Score; AIS, Abbreviated Injury Scale; LOS, Hospital Lenght of stay in days; TBI, traumatic brain injury; yrs=years.

Between 1 week and 3 months, the percentage of patients who reported problems on the 'pain/discomfort' and 'self-care' dimensions of the EQ-5D decreased steeply. For the 'mobility' and 'usual activities' dimensions, this decrease started after 1 month after trauma. The percentage of patients who reported problems on the 'anxiety and depression' dimension was the highest at 1 month after trauma. Within 6 months post-trauma, patients showed most recovery. From 6 months post-trauma onwards, little improvement in overall HS was found. The percentage of patients who reported improvements on the different EQ-5D domains increased up until 24 months. However, the vast majority of trauma patients did not recover to their pre-injury HS. At short-term (up until 1 month post-trauma) female gender, lower extremity, spine, shoulder and upper arm injuries, injury severity, comorbidities and a longer hospital stay were associated with lower HS. At mid-term (3 and 6 months), almost the same prognostic factors were significant and relevant, however, only injury severity seemed to be less important. At the long-term a high age, two or more comorbidities, longer hospital stay and only a few injuries (i.e. lower extremity fracture and spine injury) showed a significant lower HS. The effect of injury severity seemed to fade out over time. Spinal cord injury patients had the highest risk (long-term Beta -0,18, CI -0,27;-0,08) on a lower HS during both the short (not significant), mid and long-term post-trauma. Middle and high educational level was associated with a higher HS on the long-term compared to those with low educational level. The prevalence rates of symptoms of anxiety and depression were relatively low. In contrast, symptoms of post-traumatic stress were highly prevalent and were present five times as often as compared with the Dutch general population (45).

Most recovery in HS occurs up until 3 months post-trauma, which is in agreement with previous studies on this topic (7, 9, 18). In this regard, the addition of an assessment at 1 week post-trauma in the present study adds detailed insight into (baseline) functioning shortly after trauma. Thereby, it provides a more valid assessment of the magnitude of recovery. Prior work also confirms the finding that a large proportion of patients have a considerable lower HS at 1 year post-trauma compared to pre-injury HS (7, 10, 15) or compared to the HS of the general population (46).

Besides the physical injury itself, other characteristics largely affect HS after trauma, in particularly at the long-term. This finding extend those of previous studies (14, 33), confirming that patients who were the most severely injured, were not automatically those with the lowest HS.

In this study, prevalence of symptoms of anxiety and depression were slightly higher compared to the prevalence of an anxiety disorder or depression of the Dutch population (both disorders are estimated to be present in 10.0% of the Dutch population) (47, 48). As a result, prevalence of symptoms of anxiety and depression slightly decreased over time. Prior recent and comparable studies documented slightly higher prevalences of symptoms of anxiety and depression (7, 15).

Prevalence of symptoms of post-traumatic stress were high as compared with the Dutch population (15.6% at 1 week post-trauma versus 2.6-3.3%) (45). Our prevalence rate of long-term symptoms of post-traumatic stress are in line with previous research that also uses the ≥35 cut-off point of the IES (12). Though, the systematic review by Haagsma *et al.* (49) revealed prevalences of post-traumatic stress in hospitalized trauma patients that ranged from 30% (90% CI 27%-33%) within 3 months post-trauma to 6% (90% CI 4%-10%) at 1 year. Compared to those results, we found a lower prevalence of symptoms of post-traumatic stress early post-trauma whereas a higher prevalence was found at 1 year of follow-up. This discrepancy may be due since studies used various instruments and different cut-off points to indicate post-traumatic stress.

This study was conducted according to the recommended guideline of measuring non-fatal outcome after trauma (39). The BIOS included a broad study population, measured both short-term and long-term outcomes, measured functioning prior to the trauma, included a large number of patient and injury-related characteristics and proxy informants were asked in patients who were incapable to complete the set of questionnaires themselves. Recruitment for the BIOS occurred in all hospitals of the Dutch Noord-Brabant region, covering both urban and rural populations.

However, this study also has its limitations. First, there was non-response bias since younger patients, elderly, patients with very minor injuries (ISS 1-3) and those with a low status score (used as a proxy to indicate SES) were less likely to participate. Apparently, it is a challenge to include these specific groups. Previous studies also reported lower response rates in younger and elderly patients (5, 9, 23, 33), in patients with minor injuries (9) and those with low educational level (50, 51). Second, only a selected group of patients (18% of the eligible population) completed the first week assessment. Since most recovery occurs within the first 3 months post-trauma, it is vital to examine very early recovery patterns. This study provides unique data since the use of the standardized 1 week assessment in a comprehensive group of trauma patients. Nevertheless, in most cases, non-responders at this time point felt too disabled to respond to complete a long questionnaire. Therefore, this most probably led to an underestimations of the reported HS and psychological outcomes at 1 week post-trauma.

Since the acute character of a trauma, it is difficult to include patients soon after their trauma in order to examine very early recovery patterns. In order to increase response rate and to reduce loss to follow-up, future research should minimize the large amount of questionnaires that patients have to complete at each time point, especially early post-trauma. A promising technique includes computerized adaptive testing (CAT). In this already proven valid technique, tailored-made short and precise domain-specific data can be collected (52-55).

We are aware that recall bias and response shift most probably led to an overestimation of the pre-injury HS as measured in this study. Though, to produce valid estimates of the health impact and the decrease of functioning after trauma, information on patients functioning prior to the trauma is crucial (56-59). Future research should focus on the effects of recall bias and response shift on retrospectively collected data.

According to the literature, early recognition, treatment and monitoring of psychological problems improve non-fatal outcome after trauma (15, 60-63). Therefore, early screening and interventions to reduce post-traumatic stress should be part of standard care. Furthermore at long-term, patients aged ≥75 years, patients with a longer length of hospital stay and patients with ≥2 comorbidities are more likely to have a poor HS. For these patients, standard aftercare should be extended to screen on remaining problems that the patients have to address after their trauma, e.g. by a follow-up appointment with a case manager.

CONCLUSION

Hospitalized trauma patients experience substantial reductions in HS and reported frequently symptoms of post-traumatic stress. Most improvements in HS and psychological symptoms occurred within the first 3 months post-trauma. After two years post trauma, the vast majority of trauma patients did not achieve their pre-injury HS. Recovery trajectories varied widely in which

female gender, age ≥75 years, spinal cord injury, having more comorbidities, low educational level, and a longer hospital stay are associated with higher risk on decreased HS at long-term after trauma. At short-term also several lower extremity injuries are prognostic factors for decreased HS.

ACKNOWLEDGEMENTS

Membership list of the BIOS-group: P.V. van Eerten, F.C. van Eijck, H.J. van Geffen, W.A. Haagh, L.M. Poelhekke, J.B. Sintenie, C.T. Stevens, A.H. van der Veen, C.H. van der Vlies, D.I. Vos.

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Appendix 3.A: Injury group classification of the most common types of injury, based on the Abbreviated Injury Score (64)

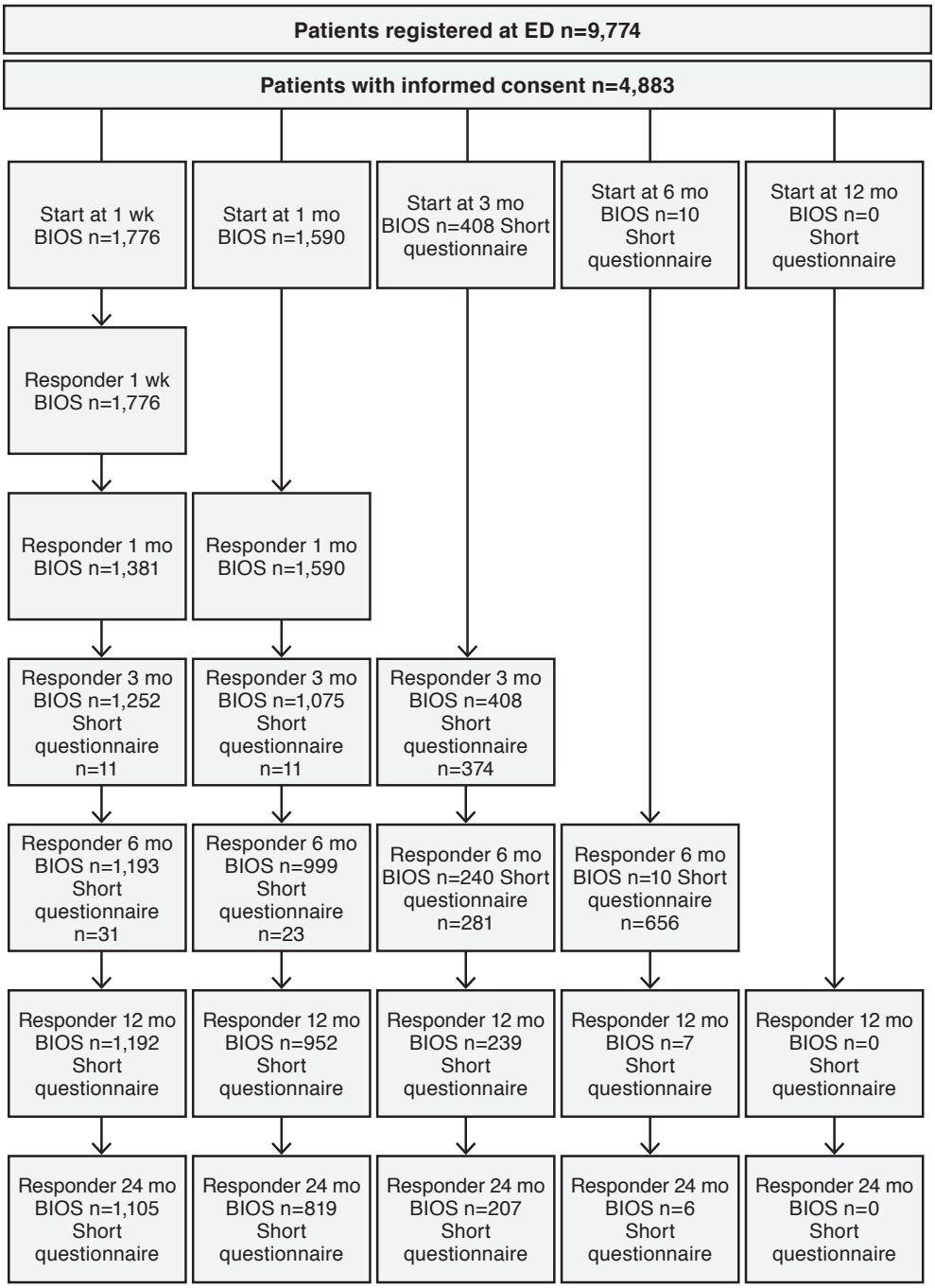
Type of trauma	First three numbers of the AIS-code	Injury severity (.1=minor, .6=maximal)
Pelvic injury	856	.2, .3, .4, .5
Hip fracture	853	.3
Tibia, complex foot or femur fracture	854	.2
	857	.2
	858	.2
Shoulder and upper arm injury	770	.1, .2
	771	.1, .2
	750	.2
	751	.2
Radius, ulna or hand fracture	752	.1, .2, .3
	753	.2
Mild TBI	110	.1, .2
	140	.2
	161	.1, .2
Severe TBI	110	.3
	140	.3, .4, .5, .6
	161	.3, .4, .5
Facial fracture	250	.1, .2, .3
	251	.1, .2, .3
Thoracic injury	441	.1, .2, .3, .4, .5
	419	.2, .3, .4, .5
	442	.2, .3, .4, .5
Rib fracture	450	.1, .2, .3, .4
Mild abdominal injury	516	.1, .2
	510	.1, .2
	521	.2
	530	.1
	540	.1, .2
	541	.2
	542	.1, .2
	543	.1, .2
	544	.1, .2
	545	.1, .2
Severe abdominal injury	516	.3
	510	.3
	520	.3
	520	.4, .5
	521	.3, .4
	540	.3, .4
	541	.3, .4, .5
	542	.3, .4, .5
	543	.3, .4, .5
	544	.3, .4, .5
	545	.3, .4, .5
Spinal cord injury	640	3, .4, .5
Stable vertebral fracture or disc injury	650	.2, .3

Abbreviations: AIS, Abbreviated Injury Score; TBI, traumatic brain injury.

Appendix 3.B: Methods of imputed data of the Brabant Injury Outcome Surveillance

Missing Abbreviated Injury Scale codes for the participants were manually checked in the electronic patient files, resulting in almost complete data for the ISS (0.9% missing). If at least half of the items of the Hospital Anxiety and Depression Scale (HADS) were completed, missing items were imputed using the individual subscale means according to the half-rule (65). We assumed that missing values were missing at random (MAR) (66). The imputation model included demographic and injury-related characteristics as well as summary scores of the questionnaires. Variables included in the imputation model were: name of the hospital in which the patient was admitted, age at the day of the trauma, gender, deceased during the study period, work prior to the trauma, patient aged ≥65 with a hip fracture, emotional well-being 1 day prior to the trauma (Health Utilities Index Mark 2 (HUI2) question 3 and Health Utilities Index Mark 3 (HUI3) question 6), the use of a walking aid 1 day prior to the trauma (HUI3 question 4), whether the questionnaires were completed by a proxy informant or not, cause of trauma, mode of transport to the hospital, hospital length of stay, Intensive Care Unit admission, comorbidities, Injury Severity Score, discharge destination, and the summary scores of the (pre-injury) EuroQol-5D-3L, (pre-injury) EuroQol Visual Analogue Scale, (pre-injury) Groningen Frailty Index, HUI2, HUI3, HADS subscale anxiety, HADS subscale depression, Impact of Event Scale, ICEpop CAPability measure for Older people and the Oxford Hip Score questionnaires collected at time points up until 1 year post-trauma. Imputed values for patients who did not participate at that specific follow-up questionnaire were back-transformed into missing values.

Appendix 3.C: Number of participants throughout the Brabant Injury Outcome Surveillance (n=4,883)



Abbreviations: ED, emergency department; BIOS, Brabant Injury Outcome Surveillance; wk, week; mo, months.

4

Chapter

The effect of socio-economic status on non-fatal outcome after injury: A systematic review

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Injury 2017;**48**:3
DOI: 10.1016/j.injury.2017.01.013

ABSTRACT

Background: Over the past decades, the number of survivors of injuries has rapidly grown. It has become important to focus more on the determinants of non-fatal outcome. Although socio-economic status (SES) is considered to be a fundamental determinant of health in general, the role of SES as a determinant of non-fatal outcome after injury is largely unknown.
Methods: An online search was conducted in November 2015 using Embase, Medline, Web of Science, Cinahl, Cochrane, Google scholar and PubMed. Studies examining the relation between SES and a physical or psychological outcome measure, or using SES as a confounder in a general trauma population were included. There were no restrictions regarding study design. The 'Quality in Prognostic Studies tool' was used to assess the methodological quality of the included studies.
Results: The 24 included studies showed large variations in methodological quality. The number of participants ranged from 56 to 4,639 and assessments of the measures ranged from immediately to 6 year post-injury. Studies used a large number of variables as indicators of SES. Participant's educational level was used most frequently. The majority of the studies used a multivariable technique to analyse the relation between SES and non-fatal outcome after injury. All studies found a positive association (80% of studies significant, n=19) between increased SES and better non-fatal outcome after injury.
Conclusion: Although an adequate and valid measure of SES is lacking, the results of this review showed that SES is an important determinant of non-fatal outcome after injury. Future research should focus on the definition and measurement of SES and should further underpin the effect of SES on non-fatal outcome after injury.

Keywords: injury, trauma, socio-economic status, socioeconomic status, determinant, physical outcome, physiological outcome, non-fatal outcome

INTRODUCTION

Injuries continue to be a tremendous burden on public health and disproportionately affects poor, young and older populations (1). Over the past decades, the number of survivors of injuries has rapidly grown due to major advances of modern injury care (2, 3), resulting in a shift in attention from fatal towards non-fatal injury survivors. Disability due to injuries has not reduced, leading to a growing number of injury patients with long-term disabilities (4-8).

The majority of the injury survivors experience short-term or long-term impairments or disability, which affects their health-related quality of life (HRQoL) (9) and inhibits them to return to full employment (10). Furthermore, functional outcome more than one year post-injury, is often far below population norms (5, 8). Therefore, it has become important to focus on the determinants of non-fatal outcome after injury (11). According to the literature there is a wide range of possible parameters to determine patients' physical and psychological functioning after injury. These determinants include injury-related factors (e.g. mechanism, type of injury or injury severity), comorbidity, social support, self-efficacy or demographic characteristics (e.g. age or gender) (3, 8, 12-19).

Socio-economic status (SES) is considered to be a fundamental determinant of health and an important characteristic of both human and environmental factors. SES is defined as *'a hierarchical continuum according to prestige, lifestyle, attitudes and values, which define a person's position in society '* (20). Previous studies indicated that people with a low level of SES are overrepresented in the injured population (21, 22). Currently, educational level and income are often used to determine SES in medical research (23, 24). Despite its fundamental role, the effect of SES inequalities on non-fatal outcome after injury are considered complex. Both individual and environmental factors play an important role (25); for instance psychological factors (e.g. poverty-related stressors), material resources (e.g. decent housing), health behavior (e.g. smoking) or work and occupational exposure (e.g. working condition) might contribute to physical and psychological outcome after injury.

In 2002, Cubbin *et al.* (1) aimed to critically examine the methods that were used to measure and interpret SES in studies of fatal and non-fatal outcome after injury. Cubbin *et al.* reviewed 53 studies on SES and injury risk. The authors concluded that increasing SES has a strong inverse association with the risk of homicide and fatal unintentional injuries although the results for suicide were mixed. The effect of SES on non-fatal injuries was less consistent than for fatal injuries. However many of the included studies utilized arbitrary measures of SES and measures were often inadequately defined. The interpretation of the role of SES was lacking in the included studies.

Although SES is a fundamental determinant of outcome after injury (26-29), little attention has been paid to SES in the public health literature focusing on injury control and prevention. Studies are often restricted to specific types of injuries (e.g. traffic injuries or traumatic brain injury (30, 31)) or particular age groups (e.g. children or adolescents (32, 33)), so definite conclusions about the effect of SES on non-fatal outcome for the general trauma population are difficult to draw.

A growing number of patients have to deal with long-term consequences after injury. Knowledge of the role of SES may influence psychological and physical outcome of injury survivors.

To our knowledge this is the first systematic review that examined the effect of SES on non-fatal outcome after injury for the general injured population. The main objective is to summarize the current knowledge of the effect of SES on non-fatal outcome after injury. Another aim is to critically examine the measurements and interpretations of SES of the included studies.

METHODS

Data sources

Peer-reviewed studies that were published until November 2015 were included: Embase (4,752 hits), Medline Ovid (1,036 hits), Web of Science (713 hits), Cochrane (20 hits), PubMed (316 hits) and Google Scholar (248 hits). All selected studies were downloaded to RefWorks (34) and duplicates were removed. The following key words were used: 'injury'; 'trauma'; 'socio-economic status'; 'social class'; 'income'; 'education'; 'recovery'; 'outcome'; 'disability'; '(health-related) quality of life' and 'health status'. See **Appendix 4.A** for an overview of all search terms.

Study selection

Studies were included in the review if they were published in English in a peer-reviewed journal up to November 3rd 2015. This review focused on 'all injury' studies (i.e. representing a general trauma population) irrespective of injury severity. Studies with a mixed age population (e.g. adolescents and adults) were included as well. Injury was defined according to the World Health Organization (WHO) as *'relatively sudden discernible effects due to body tissue damage from energy exchanges or ingestion of toxic substances but not due to medical adverse events and obtained from health care settings'*. Only patients with an injury seen on the emergency department (ED) of a hospital were included. SES was based on individual level (e.g. educational level or income) or based on area level (e.g. deprivation of an area). Studies were included if patients' post-injury physical and/or physiological functioning was measured. To meet the inclusion criteria, analyses of SES with the outcome measure had to be performed. Studies that examined fatal and non-fatal outcome were only included if data of the non-fatal outcome was analysed separately. We excluded studies that focused on specific types of injuries (e.g. traumatic brain injury or burns) or studies that included only children or adolescents. There were no restrictions regarding the type or design of the study.

If more than one article was written based on the same study data (i.e. multiple publications), one main article was selected based on the following criteria: (1) the study that described the effect of SES on a physical of physiological outcome measure; (2) the study with the largest number of included patients. Any other articles based on the same study database were used to extract any additional information or determinants.

Studies were screened on title and abstract. The output of the searches and screening are reported in the PRISMA study Flow Diagram (35) (see **Figure 1**). One author (NK) screened all titles that were identified in the searches to determine whether they were eligible for inclusion or not. Two authors (NK and SP) independently screened all abstracts. At the same time, statistical analyses as reported in the full-text were screened to determine whether the relation between SES and a physical or physiological outcome measure was analysed if this was not reported in the abstract. Finally, articles were screened full-text. The same two authors hand-searched reference lists of selected articles (reference and author tracking). Any disagreement was resolved by discussion until consensus was reached or by consulting a third author (MJ).

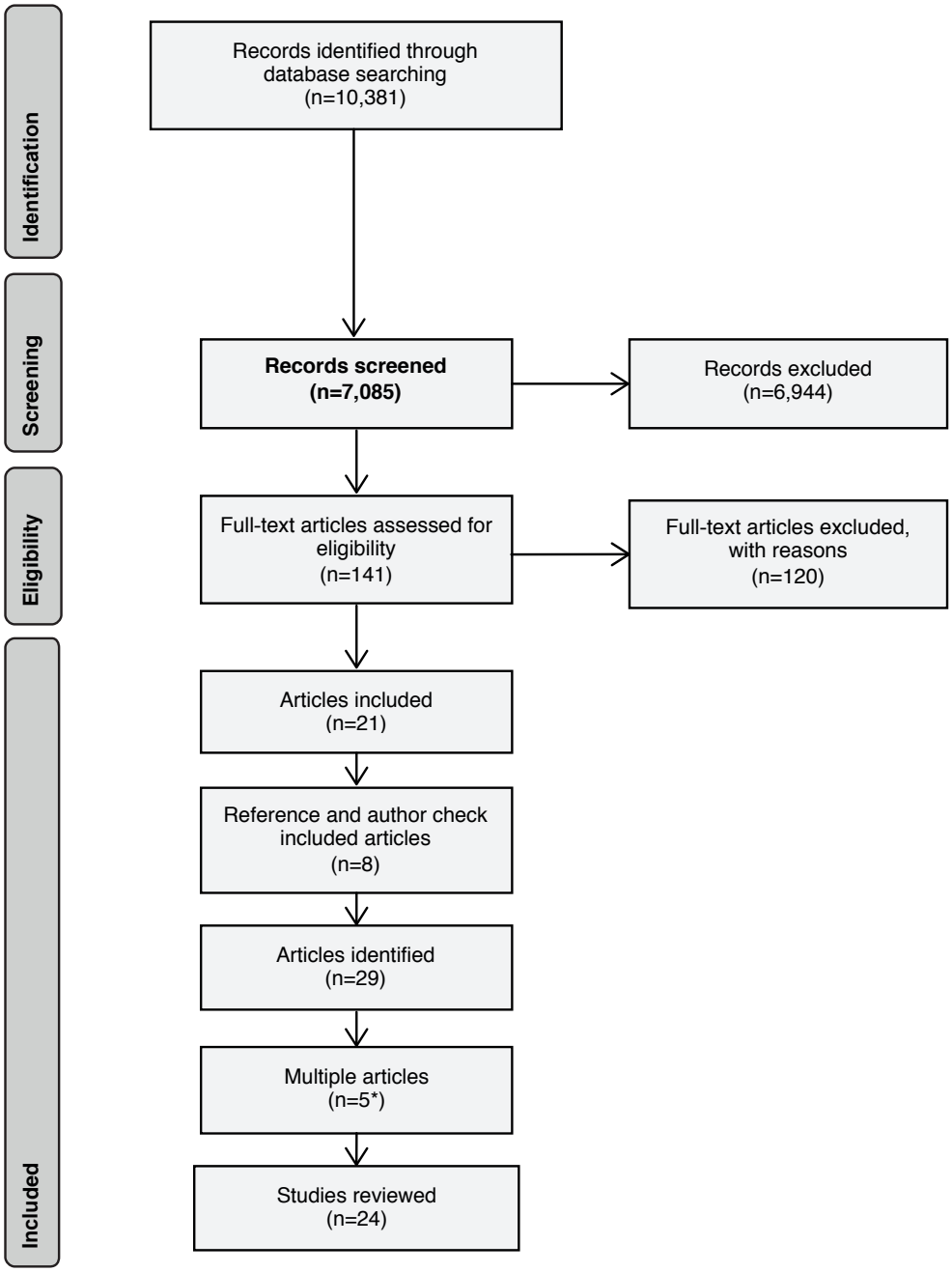

Figure 1: Prisma Flow diagram of the included studies in the systematic review
*The articles of Harris *et al.* (45,50), Holbrook *et al.* (8,19,51) and Holmes *et al.* (46,57,58) used the same data set, therefore these articles were considered one.

Data extraction and quality assessment

The two authors (NK and SP) independently extracted the data and assessed the risk of bias of the included studies. Any discrepancies were resolved via discussion until consensus or by consulting a third author (MJ). A data extraction template in MS Excel was developed and piloted for the review. Details from this data extraction form were used to devise summary tables for each included study.

The methodological quality of the studies was assessed by using the 'Quality in Prognostic Studies tool' (QUIPS) (36). The QUIPS is a recently developed tool to assess the risk of bias in prognostic factor studies. The QUIPS considers six criteria to determine the external validity of a study, i.e. study participation, study attrition, prognostic factor measurement, outcome measurement, study confounding, and statistical analyses and presentation. Each criterion is rated as low risk, moderate risk or high risk. The same two authors independently used the checklist to rate the studies. Any discrepancies in completing the QUIPS were resolved via discussion until consensus or by consulting a third author (MJ).

RESULTS

Study selection

We identified 7,085 titles of potentially relevant articles. After screening the titles, 6,944 articles were excluded. These were mainly excluded from the review because the role of SES as a determinant was studied in a specific injured population (e.g. burns). Of the remaining 141 articles, 120 were excluded after both reading the abstract and after screening the statistical analyses as reported in the full-text. An extensive number of the articles were excluded in this step since there was no association studied between SES and psychological or physical outcome. Twenty-one articles were included after the literature search (4, 6, 10, 19, 37-53). By reference and author tracking of the included articles, eight additional articles were identified and included in the review as well (3, 8, 54-59) resulting in twenty-nine articles.

Eight of these articles published about three studies, so five multiple publications were identified: the articles of Harris *et al.* (45, 50), Holbrook *et al.* (8, 19, 51) and Holmes *et al.* (46, 57, 58). Finally, 24 studies were included in the systematic review. See **Figure 1** for more details.

Measurement of SES

As shown in **Table 1**, SES is a broad concept. The included studies used different methods. SES was determined by a single variable, two or more variables and multiple variables were used separately or were combined to form an index. Almost all studies used individual-based SES (e.g. educational level) (n=21). One study used area-based SES (zip code) and two studies used a SES index.

Table 1: Concepts of socio-economic status (SES) of the included studies

Author, year	n	Individual-based SES	Area-based SES	SES index
Abedzadeh-Kalahroudi *et al.* (2015) (37)	400	Edu level; Not reported		
Attenberger *et al.* (2012) (59)	117	Edu level; High educational level n=56		
Chiu *et al.* (2011) (47)	527		Zip code to determine mean household inc: mdn $40,598	
Connelly *et al.* (2006) (40)	3,824	Edu level; Not reported		
Gabbe *et al.* (2012) (38)	3,824	Edu level; Not reported		
Glancy *et al.* (1992) (6)	441	Edu level; <baccalaureate degree; 376		
Gross *et al.* (2011) (39)	102	Edu level; Not reported		
Harris *et al.* (2007, 2008) (45, 50)	355	Edu level and annual inc: Primary; 8.6%: secondary; 54.2%: certificate/diploid; 28.7%: bachelor degree; 8.6%. Inc: $0–30,000; 46.4%: $30,000–50,000; 24.1%: $50,000–75,000; 15.7%: ≥$75,000; 13.9%		
Holbrook *et al.* (1998, 1999, 2001) (8, 19, 51)	1,048	Edu level and income; 85% ≥HS edu: 41% annual inc >$20,000		
Holbrook *et al.* (1994) (52)	63	Edu level; 48% (n=20) ≥HS edu, n=22 <HS edu		
Holmes *et al.* (2010a, 2010b, 2013) (46, 57, 58)	290	Edu level and income: Not reported		
Holtslag *et al.* (2007) (4)	335	Edu level: Primary school n=56, higher edu n=277		

Table 1 *(continued)*

Author, year	n	Individual-based SES	Area-based SES	SES index
Janssen *et al.* (2009) (41)	90			Helmert-Index: mean 15.8 (±4.7, range 5–25)
Kendrick *et al.* (2013) (42)	1,517			Townsend deprivation index: deprivation, tertiles: 5–17y (n = 298): (1.) (least deprived) 38.3%: (2.) 29.7%: (3.) (most deprived) 32.1%. 18–64y (n = 914): (1.) 31.8%: (2.) 33.1%: (3.) 35.1%. 65+ y (n = 305): (1.) 36.8%: (2.) 34.0%: (3.) 29.2%
Langley *et al.* (2011) (54)	2,856	Edu level and income; Highest edu qualification: none; 15%, secondary school; 24%, post-secondary school; 59%. Financial status: insufficient; 9%, sufficient; 89%		
MacKenzie *et al.* (1988) (3)	597	Edu level; Grades 1–8: 7.8%, grades 9–11: 31.8%, HS graduate: 40.6%, college: 19.8%		
Meerding *et al.* (2004) (10)	4,639	Edu level; Not reported		
Michaels *et al.* (1998) (55)	56	Edu level and annual inc; 74% HS edu, 25% of these had a college degree. Inc: mean $29,700 (±2,180) p/y		

Table 1 *(continued)*

Author, year	n	Individual-based SES	Area-based SES	SES index
Rainey *et al.* (2014) (44)	110	Edu level and annual inc: ≥8th grade; 2.7%: 9th-12th grade; 18.0%: HS diploma; 32.4%: Some college credits; 2.7%: Associate's degree; 10.8%: Bachelor's degree; 22.5%: Some credits of master's degree; 0.9%: Master's degree; 7.2%: Some credits of doctoral degree; 0.9%: Doctoral degree; 0.9%. Inc: <$25,000; 24.3%: $25,000–$49,000; 11.7%: $50,000–$74,000; 18.9%: >$75,000; 23.4%: Unobtainable; 19.8%		
Ringburg *et al.* (2011) (49)	246	Educ level: Primary school n=45, higher edu n=181		
Sirois *et al.* (2009) (53)	1,092	Edu level: 1–7y: 9.8%; 8–12y: 51%; 13–15y: 23%; >15y: 16.2%		
Sluys *et al.* (2005) (56)	146	Edu level: HS education 68%, of these, 17% had college degrees and 10% had postgraduate university degrees		
Sorensen *et al.* (2008) (43)	3,798	Edu level; Not reported		
Trost *et al.* (2015) (48)	155	Edu level and annual inc: <HS; 18.7%: HS diploma; 33.5%: Associate's; 12.3%: Bachelor's; 23.2%: Graduate/professional; 6%: Would rather not say; 1.3%. Inc: <$25,000; 24.5%: $25,0000–49,000; 10.3%: $50,000–74,000; 18.7%: >$75,000; 25.2%: Not sure/would rather not say; 21.3%		

Abbreviations: SES, socio–economic status; edu, education(al); HS, High School; inc, income; mdn, median; p/y, per year; y, year.

Individual-based SES

Individual-based SES was used in 21 studies, of which 13 used patient's educational level. In five studies, demographic characteristics concerning the educational level of the included patients were not reported in the result section. Eight studies used a combination of patient's educational level and annual income to determine SES. In two studies the demographic characteristics of educational level and income were not reported in the result section.

To determine individual-based SES, almost all studies used one or more cut-off points for educational level and income. For educational levels, High School (HS) as a cut-off point was used the most frequently. One study (53) determined SES via the number of completed educational years. Regarding patient's annual income, studies used various cut-off points, except for the study of Langley *et al.* (54) in which patients were asked whether their financial status was sufficient or not.

Area-based SES

In the study of Chiu *et al.* (47) patients' zip codes were used to determine SES. The zip codes were used to determine mean household income based on the U.S. Census Bureau Data.

SES index

Two studies used a SES index. The study of Janssen *et al.* (41) used the Helmert Index. This index is calculated based on the patient's educational level, occupational position and household net income per capita (60, 61). The study of Kendrick *et al.* (42) used the Townsend deprivation index which is based on a patient's zip code and information about a patient's accommodation type, number of rooms and number of people and cars in the household (62).

Study characteristics

Most studies that were included in the review had a prospective design and were published after 2006. The majority of the studies used a cross-sectional design and the remaining studies used a longitudinal design. The number of participants varied between 56 (55) and 4,639 (10). All studies included a population with 'general trauma'. However, in seven studies a cut-off point of injury severity (Injury Severity Score (ISS)>15) was applied and two studies only included polytrauma patients (≥2 Abbreviated Injury Scale (AIS)-regions and ISS>16). Most studies included only adult patients. See **Table 2** and **3** for detailed information per study.

Table 2: Study characteristics of studies examining the effects of socio-economic status (SES) on physical or psychological functioning after injury: generic injury population

Author, year	Design, setting	n	Population and patient characteristics	Outcome measure and assessment	Statistical analysis	
					Univariate	Multivariate
Generic injury population						
Abedzadeh-Kalahroudi *et al.* (2015) (37)	Longitudinal FU study, Iran	400	15–65y (34.4y (±14.6), 84.2% male), no physical/mental disability, LOS hospital >24h. Excl.: not available during FU	WHODAS II *(disability):* 3mo	n.a.	Logistic Regression OR: 1.425 (95% CI: 0.862, 2.356)
Chiu *et al.* (2011) (47)	Prospective study, USA	527	≥18y (mdn 39.0y, 71.7% male), admitted to hospital. Excl.: no English speaking, self-inflicted injury, unable to communicate	PTSD Check-list-Civilian *(PTSD):* Immediately post-injury	Spearmans' rank correlation Household inc–PCLC: r=-0.23 (p<0.01)*	Linear regression Inc β=0.001* and β-adjusted=0.117*
Glancy *et al.* (1992) (6)	Prospective FU study, USA	441	18–64y (32.7y (±11.70), % male: not reported), admitted to injury service ≥24h, mentally able to complete questionnaires, discharged home	Resumption of usual level of activity *(return to function):* 1.5, 3, 6mo	n.a.	Log-linear proportional hazards regression <HS (reference), HS graduate, RHR: 1.07 (NS). Some college, RHR: 1.41 (NS), ≥college, RHR: 1.88 (p=0.002)*
Holbrook *et al.* (1998, 1999, 2001) (8, 19, 51)	Prospective study, USA	1,048	≥18y (36y (±14.8), 70% male), GCS admission ≥12, LOS hospital ≥24h, corresponding phone number for FU contact, English or Spanish speaking	**1998, 1999:** QWB *(HRQoL):* Discharge, 6, 12, 18mo **2001:** IES *(acute stress):* Discharge, 6, 12, 18mo	χ^2-test **2001:** Edu: high school+: (NS). Inc (p<0.05)*. **1999:** Education (<HS vs. HS+): OR:1.8 (p<0.05)*. Inc (<$20,000 vs. >$20,000): OR: 1.1 (NS)	Normal least squares Regression **1998:** 6mo: mean and mean % change QWB. <HS: change: 54.1% (p<0.05)*. HS+: change: 60.9% (NS) Inc: <$20,000: change 56.4% (p<0.001)*, $20,000+: change 64.5% (NS). % change QWB: edu: β=-4.99 (NS). Inc: β=-4.31 (NS). Age-adjusted OR: Edu: OR: 2 (p<0.05)*, inc: OR: 2.1 (NS). **1999:** 12mo: mean QWB: edu (p<0.001)*, inc (p<0.001)*

Table 2 *(continued)*

Author, year	Design, setting	n	Population and patient characteristics	Outcome measure and assessment	Statistical analysis	
					Univariate	Multivariate
Holbrook *et al.* (1994) (52)	Prospective study, USA	63	≥18y (30y (±13.1), 74% male), GCS admission ≥12, LOS hospital ≥24h, current San Diego County address and phone number. Excl.: military service, prisoners	QWB *(HRQoL):* Pre-discharge, 3mo	Risk factor analysis Edu: <HS vs HS+, % change in QWB (tertile group): RR=0.8 (NS)	Normal least square regression 3mo: Model 1: FU QWB. Edu (<HS vs. HS+): β=-0.0616 (NS). Model 3: % change in QWB over baseline. ED (<HS vs. HS+): β=-7.2272 (NS)
Holmes *et al.* (2010a, 2010b, 2013) (46, 57, 58)**	Prospective (FU) cohort study, Australia	290	18–70y (38.5y (±13.1), 75.9% male), at least one AIS≥ 2, hospital LOS ≥24h, adequate English, assessed within 14/15d-30d of injury. Excl.: non-height fall injury, moderate-severe head injury, psychotic, suicidal, cognitive impairment	**2010a, 2010b:** Pain severity and chronic pain. **2013:** item 8 of the SF-36, pain-related disability	Pearson correlation, ANOVA or χ^2-test **2010a:** Association with pain severity: Edu: Secondary vs tertiary (NS). Inc: <$60,000 vs ≥$60,000 (NS). **2010b:** Association with pain severity: Edu: Secondary vs tertiary (NS). Inc: <$60,000 vs ≥$60,000 (NS). Association with chronic pain: Edu: Tertiary (NS). Inc: <60,000 (NS). **2013:** Association with chronic pain. Edu: Tertiary (NS). Inc: >$90,000 (p=0.003)*	Logistic regression **2013:** Association with chronic pain. Inc: OR: 4.01 (95% CI: 1.23, 12.40)*
Janssen *et al.* (2009) (41)	Controlled, randomized and prospective study, Germany	90	18–75y (42.3y (±12.9), 74.4% male), ≥2 injuries (reaching a total AIS>6), mentally orientated. Excl.: severe cranial injury, suicide, violent crimes victims, mental disorder, no German speaking	*Self-reported health*: excellent, very good, good, fair, or poor, mean 3.7y (±1.5), range 0.7-5.9y. STAI X-1 *(anxiety):* ICU–normal ward: after transfer	Pearson correlation Self-related health vs SES: r=0.191 (NS). STAI X-1vs SES: r=-0.028 (NS)	Linear regression **Outcome self-related health. Step 1:** SES: β=0.210 (p=0.049)*. **Step 2:** SES: β=0.208 (p=0.052). **Step 3:** SES: β=0.214 (p=0.022)*

Table 2 *(continued)*

Author, year	Design, setting	n	Population and patient characteristics	Outcome measure and assessment	Statistical analysis	
					Univariate	Multivariate
Kendrick *et al.* (2013) (42)	Prospective longitudinal study, GB	1,517	≥5y (<18y: 60%; 18–64y: 20%; >65y: 20%, 54% male), attending ED or admitted to hospital with any type of injury, patient or proxy able to give consent and to complete questionnaires. Excl.: No permanent address	*Self-reported recovery*: yes or no, 1, 4, 12mo or until recovery	Modified Poisson regression (in tertiles; tertile 1 is reference group) **Factors associated with recovery: 5–17y** 1mo recovered: deprivation: Tertile 2. RR: 1.30 (95% CI 0.96, 1.76). Tertile 3. RR: 1.17 (95% CI 0.85, 1.61). 4mo recovered: deprivation: Tertile 2. RR: 1.15 (95% CI 0.97, 1.36). Tertile 3. RR: 1.05 (95% CI 0.87, 1.28). 12mo recovered: deprivation Tertile 2. RR: 1.03 (95% CI 0.93, 1.15). Tertile 3. RR: 0.96 (95% CI 0.84, 1.10). **Factors associated with recovery: 18–64y:** 1mo recovered: deprivation: Tertile 2. RR: 0.96 (95% CI 0.67, 1.38). Tertile 3. RR: 0.96 (95% CI 0.66, 1.41). 4mo recovered: deprivation: Tertile 2. RR: 0.96 (95% CI 0.75, 1.22). Tertile 3. RR: 1.11 (95% CI 0.88, 1.39). 12mo recovered: deprivation: Tertile 2. RR: 0.98 (95% CI 0.83, 1.16). Tertile 3. RR: 1.00 (95% CI 0.84, 1.18). **Factors associated with recovery: ≥65y:** 1mo recovered: deprivation: Tertile 2. RR: 1.13 (95% CI 0.59, 2.16). Tertile 3. RR: 1.01 (95% CI 0.49, 2.08). 4mo recovered: deprivation, tertiles: Tertile 2. RR: 1.20 (95% CI 0.81, 1.78). Tertile 3. RR: 1.04 (95% CI 0.65, 1.64). 12mo recovered: deprivation, tertiles: Tertile 2. RR: 1.25 (95% CI 0.93, 1.68). Tertile 3. RR: 1.02 (95% CI 0.71, 1.45)	n.a.

Table 2 *(continued)*

Author, year	Design, setting	n	Population and patient characteristics	Outcome measure and assessment	Statistical analysis	
					Univariate	Multivariate
Langley *et al.* (2011) (54)	Prospective cohort study, New Zealand	2,856	18–64y (18–24y: 14%; 25–44y: 43%; 45–64y: 43%, 61% male), referred to Accident Compensation Corporation for case co-ordination and/or management for acute injury. Excl.: self-harm, genderual assault	EQ-5D + cogn. dimension *(HRQoL):* 3.2mo	Descriptive statistics **Prevalence: Highest edu level:** None: Mobility; 42% (95% CI: 38, 47), self-care; 27% (95% CI: 23, 31), usual activities; 55% (95% CI: 50, 60), pain, discomfort; 70% (95% CI: 65, 74), anxiety, depression; 28% (95% CI: 23, 32), cognitive; 18% (95% CI: 14, 22). Secondary school: Mobility; 40% (95% CI: 36, 44), self-care; 19% (95% CI: 16, 22), usual activities: 51% (95% CI: 47, 55), pain, discomfort; 66% (95% CI: 62, 69), anxiety, depression; 21% (95% CI: 18, 24), cognitive; 12% (95% CI: 10, 15). Post-secondary school: Mobility; 41% (95% CI: 39, 44), self-care; 25% (95% CI: 23, 27), usual activities; 55% (95% CI: 53, 58), pain, discomfort; 71% (95% CI: 68, 73), anxiety, depression; 22% (95% CI: 20, 24), cognitive; 14% (95% CI: 13, 16). **Financial status:** Insufficient: Mobility; 43% (95% CI: 37, 49), self-care; 31% (95% CI: 25, 37), usual activities; 59% (95% CI: 53, 65), pain, discomfort; 69% (95% CI: 67, 70), anxiety, depression; 34% (95% CI: 28, 40), cognitive; 21% (95% CI: 16, 26). Sufficient: Mobility; 41% (95% CI: 39, 43, self-care; 23% (95% CI: 21, 25), usual activities; 53% (95% CI: 51, 55), pain, discomfort; 74% (95% CI: 69, 80), anxiety, depression; 21% (95% CI: 20, 23), cognitive; 14% (95% CI: 13, 15)	Logistic regression Insufficient money vs mobility: OR 1.25 (95% CI: 0.89, 1.77). Insufficient money vs self-care: OR: 1.33 (95% CI: 0.96, 1.84). Insufficient money vs usual activities: OR 1.26 (95% CI: 0.94, 1.70). Insufficient money vs pain/discomfort: OR 1.34 (95% CI: 0.96, 1.87). Insufficient money vs depression/anxiety: OR 1.70 (95% CI: 1.22, 2.37)*. Insufficient money vs cognitive: OR 0.97 (95% CI: 0.60, 1.56)

Table 2 *(continued)*

Author, year	Design, setting	n	Population and patient characteristics	Outcome measure and assessment	Statistical analysis	
					Univariate	Multivariate
MacKenzie *et al.* (1988) (3)	Prospective survey, USA	597	Patients contacted for interview in hospital, over telephone at 6mo. and in person 1y (16–17y: 6.6%; 18–25y: 44.7%; 26–35y: 33.7%; 36–45y: 15.0%, 78.4% male)	Self-care, mobility and physical capabilities: 48h before dis-charge, 6mo, 1y	Descriptive statistics **Percentages working full time at 1y by functional limitations (n=262):** <$10,000, blue collar: Self-care or mobility limit; 16%, major or minor physical limit; 20%, no limit; 53%. <$10,000, white collar: Self-care or mobility limit; 33%, major or minor physical limit; 25%, no limit; 50%. ≥$10,000, blue collar: Self-care or mobility limit; 38%, major or minor physical limit; 67%, no limit; 75%. ≥$10,000, white collar: Self-care or mobility limit; 56%, major or minor physical limit; 71%, no limit; 90%. Edu, < high school: Self-care or mobility limit; 10%, major or minor physical limit; 30%, no limit; 58%. Edu, HS graduate: Self-care or mobility limit; 38%, major or minor physical limit; 50%, no limit; 71%. Edu, some college: Self-care or mobility limit; 39%, major or minor physical limit; 67%, no limit; 89%	n.a.
Meerding *et al.* (2004) (10)	FU study, the Netherlands	4,639	≥15y (15–24y: 18.4%; 25–44y: 31.8%; 45–64y: 25.0%; 65–74y: 11.7% 75–84y: 9.0%; 85+y: 4.0%, 50.6% male), visiting ED. Excl.: self-inflicted injury, institutionalized patients	EQ-5D + cogn. ability *(HRQoL):* 2, 5, 9mo	n.a.	Linear regression EQ-5D 2mo: Edu ($p<0.01$)*. EQ-5D 5mo: Edu ($p=0.08$). EQ-5D 9mo: edu ($p<0.01$)*

Table 2 *(continued)*

Author, year	Design, setting	n	Population and patient characteristics	Outcome measure and assessment	Statistical analysis	
					Univariate	Multivariate
Michaels *et al.* (1998) (55)	Prospective (cohort) study, USA	56	≥18y (35.3y (±1.75), 82% male), injury mechanism <24h, admitted to Level 1 trauma centre, absence of paralyzing spinal injury, GCS=15 within 24h of admission or extubation	Revised civilian Mississippi scale and DSM diagnosis *(PTSD):* 5mo	χ^2-test Absence PTSD: Edu in yrs: 13.9 (±0.58) (NS). Inc: $38,571 (±427) (NS) Presence PTSD: Edu in yrs: 13 (±0.68) (NS). Inc: $25,385 (±562) (NS)	n.a.
Rainey *et al.* (2014) (44)	Prospective observational study, USA	110	≥18y (46y (±18.59) , 60% male), admitted to injury service ≥24h, English or Spanish language, included in hospitals injury registry. Excl.: moderate-severe TBI, cognitive deficits	Conner-Davidson Resilience Scale: baseline. PHQ-8 *(depression):* baseline, 12mo	Pearson correlation Edu level: Baseline resilience (p=0.001)* Depression at baseline (p=0.040)* Depression 12mo (p=0.006)*	n.a.
Sirois *et al.* (2009) (53)	Population-based cohort study, Canada	1,092	18–65y (41.1y (±15.1), 64.5% male), discharged alive from acute care at level I/II injury center, required rehabilitation services. Excl.: discharge against medical advice, missing discharge destination	FIM: only physical items *(functional status)*, SF-12 *(HRQoL):* 2–4y	n.a.	Linear regression Edu vs physical FIM: β=4.51 (p≤0.05)* Edu vs aggregated Physical Score: β=2.64 (NS) Edu vs physical Function: β=3.24 (NS) Edu vs physical Roles: β=5.20 (p≤0.05)* Edu vs general health: β=3.44 (NS)

Table 2 *(continued)*

Author, year	Design, setting	n	Population and patient characteristics	Outcome measure and assessment	Statistical analysis	
					Univariate	Multivariate
Sluys *et al.* (2005) (56)	Cohort study, Sweden	146	≥15y (mdn 39y (range 20–87), 74% male), admitted to hospital, ISS ≥9. Excl.: psychiatric or cognitive disorder, no Sweden residents, language barrier, died after discharge, protected identity, in police custody, unable to contact	SF-36 *(HRQoL):* 5y	Mann-Whitney *U* test, Kruskal-Wallis test (Tukey's HSD test post-hoc) Employed full/part-time vs retired/sick leave or disability compensation: Physical functioning, role-physical, bodily pain, general health, vitality and social functioning: higher*. Role-emotional and mental health: (NS). HS vs college/university: Physical functioning, role-physical: lower*. Bodily pain: higher*. General health, vitality, social functioning, role-emotional, mental health: (NS)	n.a.
Sorensen *et al.* (2008) (43)	Multicenter prospective cohort study, USA	3,798	18–84y (47.50y (±17.72), 58.7% male), arrived alive at hospital, moderate-severe injury, identified by ICD-9 codes 800–959, ≥1 AIS ≥3 injured body area/system. Excl.: no vital signs, dead after arrival, delayed seeking treatment, major burns, ≥65y with hip fracture, non-US resident, no English or Spanish speaking, homeless or incarcerated	FCI: two questions related to sexual function: 12mo	χ^2-test, student's t-tests Edu: <HS RR: 1.54 (95% CI: 1.18, 2.01)*. HS RR: 1.52 (95% CI: 1.20, 1.93)*. College RR: 1.47 (95% CI: 1.11, 1.96)*. Post graduate: reference. Inc: <$20,000 RR: 2.32 (95% CI: 1.80, 3.00)*. $20,000–40,000 RR: 1.76 (95% CI: 1.25, 2.48)*. $40,000–60,000 RR: 1.44 (95% CI: 1.06, 1.95)*. $60,000–80,000 RR: 1.13 (95% CI: 0.79, 1.62) (NS). $>80,000: reference. Employment status: Employed: reference. Unemployed RR: 1.58 (95% CI: 1.15, 2.16)*. Retired RR: 2.03 (95% CI: 1.69, 2.45)*. Other RR: 1.67 (95% CI: 1.36, 2.06)*	Poisson regression Inc: <$20,000 aRR: 1.60 (95% CI: 1.19, 2.15)*. $20,000–40,000 aRR: 1.48 (95% CI: 1.11, 1.96)*. $40,000–60,000 aRR: 1.37 (95% CI: 1.04, 1.80)*. $60,000–80,000 aRR: 1.12 (95% CI: 0.84, 1.50). >$80,000: reference

Table 2 *(continued)*

Author, year	Design, setting	n	Population and patient characteristics	Outcome measure and assessment	Statistical analysis	
					Univariate	Multivariate
Trost *et al.* (2015) (48)	Cross-sectional study, USA	155	≥18y(47.50y (± 17.72), 58.7% male), admission to injury service ≥24h, ability to provide at least one contact for FU. Excl.: no English or Spanish speaking, cognitive deficits	Pain intensity (NRS 0-10), PHQ-8, *(depression),* PC-PTSD, VR-OCS, VR-MCS *(HRQoL):* 12mo	n.a.	Hierarchical and logistic regression analyses Pain intensity: Edu: β=-0.35 (p<0.01)*. Inc.: β=-0.23 (p<0.01)*. Depression: Edu: β=-0.029 (p<0.01)*. Inc.: β=-0.22 (p<0.01)*.Presence of PTSD symptoms: Inc: β=0.71 (p<0.05)*. Physical HrQoL: Edu: β=0.29 (p<0.01)*. Inc.: β=0.16 (p<0.01)*. Mental HrQoL: Edu: β=0.24 (p<0.01)*

*significant

**not representing a complete generic injury population

Abbreviations: AIS, Abbreviated Injury Scale; ANOVA, Analysis of Variance; aRR, adjusted relative risk; d, days; CI, confidence interval; ED, emergency department; Edu, education(al); EQ–5D, EuroQol five dimensions questionnaire; excl, exclusion; FCI, Functional Capacity Index; FIM, Functional Independence Measure; FU, follow–up; GCS, Glasgow Coma Scale; HS, High School; h, hour; ICD–9, International Classification of Diseases–9; ICU, intensive care unit; IES, Impact of Event Scale; inc, income; ISS, Injury Severity Score; limit, limitations; LOS, length of stay; mdn, median; mo., month; n.a., not applicable; NRS, Numeric Rating Scale; NS, not significant; OR, odds ratio; PC–PTSD, Primary Care PTSD; PHQ–8, Patient health questionnaire; PTSD, post–traumatic stress disorder; QWB, Quality of well–being scale; r, correlation; RHR, relative hazard ratio; RR, relative risk; SES, socio–economic status; SF–12, Short Form–12; SF–36, Short Form–36; STAI X–1, State trait anxiety inventory form X1; TBI, traumatic brain injury; VR–MCS, mental component score, part of the Veterans RAND 12–item survey; VR–OCS; physical component score, part of the Veterans RAND 12–item survey; WHODAS II, World Health Organization Disability Assessment Schedule 2.0; y, year.

Table 3: Study characteristics of studies examining the effects of socio-economic status (SES) on physical or psychological functioning after injury: severely injured population (cut off-point ISS>15 or polytrauma)

Author, year	Design, setting	n	Population and patient characteristics	Outcome measure and assessment	Statistical analysis	
					Univariate	Multivariate
Severely injured (ISS>15)						
Connelly *et al.* (2006) (40)	Population based retrospective cohort study, GB	259	≥15y (age: not reported, % male: not reported), ISS>15. Excl.: never worked	OPCS *(disability):* 5y	n.a.	Logistic regression Prognostic logistic regression OPCS 5-10 vs OPCS 0-4: Edu degree: OR: 0.014 (p=0.033)*. Edu 'O' levels and/or 'A' levels: OR: 0.288 (NS). Edu less than OA: OR: 0.246 (NS). Reduced logistic regression: Edu degree: OR: 0.068 (p=0.044)*
Gabbe *et al.* (2012) (38)	FU study, Australia	3,824	≥18y (18–24y: 17.3%; 25–34y; 14.4%; 35–44y: 13.8%; 45–54y: 13.8%; 55–64y: 11.7%; 65–74y: 10.3%; >74y: 18.7%, 71.6% male), ISS>15, blunt	GOS-E *(functional outcome):* 12mo	χ^2-test University degree (reference): OR=1.00. Advanced diploma, diploma, certificate OR= 0.65 (95% CI: 0.53, 0.80)*. Finished high school OR=0.70 (95% CI: 0.55, 0.89)*. 9-11y or equivalent: OR=0.47 (95% CI: 0.39, 0.57)*. ≤8y: OR=0.22 (95% CI: 0.29, 0.35)*	Logistic regression University degree (reference): OR=1.00. Advanced diploma, diploma, certificate OR=0.65 (95% CI: 0.53, 0.80)*. Finished high school OR=0.64 (95% CI: 0.51, 0.81)*. 9–11y or equivalent: OR=0.54 (95% CI: 0.44, 0.67)*. ≤8y: OR=0.41 (95% CI: 0.32, 0.53)*

Table 3 *(continued)*

Author, year	Design, setting	n	Population and patient characteristics	Outcome measure and assessment	Statistical analysis	
					Univariate	Multivariate
Harris *et al.* (2007,2008) (45, 50)	Cross-sectional and retrospective design, Australia	355	≥18y(47.8y (range 19–91)), 71.8%–72.1% male, major injury (ISS>15). Excl.; non-accidental injury, fatal outcome, not contactable	**2007:** *Satisfaction with progress* **2008:** SF-36, (PCS and MCS) *(HRQoL):* Between 1 and 5-6y	χ^2-test (for trend: MH) or student's *t*-test **2007:** Unadjusted association between predictors and patient satisfaction Edu: Prim.; satisfied 63.3% (NS). Sec.; satisfied 71.8% (MH) (NS). Certificate/ diploma; satisfied 74.0%*. Degree; satisfied 66.7%*. Inc: $0–30,000; safisfied 67.5% (NS). $30,001–50,000; satisfied 73.5% (MH) (NS). $50,001–75,000; satisfied 79.2%*. >$75,000; satisfied 72.9%*. Employed prior (p=0.05). Employed now (p<0.0001)*. **2008:** Unadjusted association variables and PCS/MSC. Edu–PCS (NS). ED–MSC (NS). Inc –PSC (p=0.03)*. Inc–MSC (NS). Employed pre injury–PCS (p<0.001)*. Employed pre injury–MCS (NS). Employed at FU–PCS (p<0.0001)*. Employed at FU–MCS (p<0.0001)*	Logistic regression **2007:** Unemployment OR: 2.38 (95% CI: 1.38, 4.08)*. **2008:** Employed now–PCS (p<0.0001)*. Employed now–MCS (p<0.0001)*.

Table 3 *(continued)*

Author, year	Design, setting	n	Population and patient characteristics	Outcome measure and assessment	Statistical analysis	
					Univariate	Multivariate
Holtslag *et al.* (2007) (4)	Prospective cohort study, the Netherlands	335	ISS≥16 at discharge (38y (±17), 74% male). Excl.: <16y	GOS *(functional outcome),* EQ-5D *(HRQoL),* for TBI patients: HISC *(recovery):* 12-18mo	χ^2-test, Mann-Whitney *U* test GOS-score <5: Primary school*, HS*. HISC: Primary school (NS), HS*(NS). EQvas: Primary school*, HS*. EQus: Primary school*, HS*	**Linear regression:** **Model A:** EQvas: Higher/primary school (p<0.05)*. EQus: Higher/primary school (NS). **Model B:** EQvas: Higher/primary school (p<0.05)*: EQus: Higher/primary school (NS). **Logistic regression:** Independent variable: higher/primary school. Dependent: GOS-score <5: OR: 1.1 (95% CI: 0.6, 3.6). HISC: OR: 4.5 (95% CI: 1.5, 13.0)*: EQ-mobility: OR: 2.1 (95% CI: 0.9, 5.2). EQ-self-care: OR: 1.1 (95% CI: 0.4, 2.9). EQ-daily activities: OR: 1.8 (95% CI: 0.8, 4.0). EQ-pain or discomfort: OR: 1.7 (95% CI: 0.7, 4.1). EQ-anxiety or depression: OR: 3.1 (95% CI: 1.7, 7.0)*
Ringburg *et al.* (2011) (49)	Prospective cohort study, the Netherlands	246	>14y (mdn 40y, 66% male), presented to an ED of Level I injury center, multiple injuries (ISS≥16). Excl.: dead on arrival	EQ-5D, HUI2, HUI3, EQ-VAS *(HRQoL):* 12mo	Regression (median) EQ-5D: Primary edu: 0.73 and higher edu: 0.73 (both NS). HUI2: Primary edu: 0.78 and higher edu: 0.81 (both NS). HUI3: Primary edu: 0.44 and higher edu: 0.66 (both NS). EQVAS: Primary edu: 70 and higher edu: 70 (both NS)	Logistic regression Primary school vs mobility OR: 2.0 (95% CI: 1.0, 4.2). Primary school vs self-care OR: 1.5 (95% CI: 0.6, 3.7). Primary school vs usual activities OR: 1.2 (95% CI: 0.6, 2.6). Primary school vs pain/discomfort OR: 0.7 (95% CI: 0.3, 1.5). Primary school vs anxiety/ depression OR: 0.4 (95% CI: 0.2, 1.0)*

Table 3 *(continued)*

Author, year	Design, setting	n	Population and patient characteristics	Outcome measure and assessment	Statistical analysis	
					Univariate	Multivariate
Polytrauma						
Attenberger *et al.* (2012) (59)	Validation study, Switzerland	117	≥2 AIS-regions, ISS>16, treated ≥2y (39.62y (±20.50), 75.2% male). Excl.: secondarily admitted from another hospital	Injury Outcome Profile *(QoL):* Mean 2.7y + 0.9y	Pearson correlation Edu high–depression: r=0.23 (p<0.05)*. Edu high–anxiousness: r=0.23 (p<0.05)*. Edu high–PTSD: r=0.09 (NS). Edu high–social interaction: r=0.14 (NS). Edu high–daily activities: r=0.25 (p<0.01)*. Edu level high mental functioning: r=0.20 (p<0.05)*. Edu high –body image: r=0.30 (p<0.01)*. Edu high– satisfaction: r=0.22 (p<0.05)*. Edu high–pain: r=0.28 (p<0.01)*. Edu high–function: r=0.25 (p<0.01)*	n.a.
Gross *et al.* (2011) (39)	Prospective cohort study, Switzerland	102	≥2 AIS-regions, ISS>16 (39.7y (±20.5), 74% male). Excl.; admitted secondarily from another hospital	SF-36: longer term pain, MFA: severity longer term pain: Mean 2.7y (±0.9)	n.a.	Linear regression Prevalence of longer term pain: Lesser edu level–SF36 (p=0.124) (NS). Severity of longer term pain: Lesser edu level–MFA (p=0.045)*. Lesser edu level–SF36 (p=0.015)*

*significant

Abbreviations: AIS, Abbreviated Injury Score; CI, confidence interval; ED, emergency department; Edu, education(al); EQ–VAS, EuroQol Visual Analogue Scale; EQ–5D, EuroQol five dimensions questionnaire; excl., exclusion; FU, follow–up; GOS, Glasgow Outcome Scale; GOS–E, Glasgow Outcome Scale Extended; HISC, Head Injury Symptom Checklist; HRQoL, Health–related Quality of Life; HUI2, Health Utility Index 2; HUI3, Health Utility Index 3; inc, income; ISS, Injury Severity Score; MCS, mental health component summary; mdn, median; MFA, Musculoskeletal Functional Assessment; n.a., not applicable; NS, not significant; OPCS, Office of Population Censuses and Surveys; OR, odds ratio; PCS, physical component summary; QoL, Quality of Life; r, correlation; RR, relative risk; SES, socio–economic status; SF–36, Short Form 36; TBI, traumatic brain injury; y, year.

Quality assessment

In general, the quality of the studies was moderate since in most studies a high risk of bias on the item 'study attrition' was scored and a moderate risk of bias was found on the item 'prognostic factor measurement'. Positive aspects of the included studies were the low risks of bias on the items 'study participation', 'outcome measurement', 'study confounding' and 'statistical analyses and presentation'. In two studies (4, 53) a low risk of bias was scored in all items of the QUIPS. See **Table 4** for more details.

Measurement of non-fatal outcome after injury

The included studies used a variety of instruments to asses non-fatal outcome after injury rating from a functional measure (e.g. Glasgow Outcome Scale Extended), to an HRQoL measure (e.g. EuroQol five dimensions questionnaire or the Short Form-36) or a psychological measure (e.g. Impact of Event Scale). Nine studies used more than one measure. Time assessments ranged from immediately post-injury (47) to 6 years post-injury (45, 50). Four studies did not use a standardized measure. In the study of Janssen *et al.* (41) patients were asked to rate their general health as being excellent, very good, good, fair or poor. The study of Kendrick *et al.* (42) measured functional recovery by asking patients whether their injury still affected them or not. The study of McKenzie *et al.* (3) used self-developed questionnaires concerning self-care, mobility and physical capabilities to determine patients functional limitations. Last, in the study of Harris *et al.* (50) patients satisfaction was measured by asking patients how satisfied they were with their progress since the injury.

The effect of SES on non-fatal outcome after injury

Different uni- and multivariate statistical techniques were used to determine the effect of SES on non-fatal outcome after injury. All studies concluded that a higher level of SES is associated with better outcome after injury.

In the majority of the studies both uni- and multivariate analyses were used to determine the effect of SES on non-fatal outcome. Nearly all studies found a significant association ($p<0.05$) between a higher SES level and better physical or psychological outcome on both the uni- and multivariate analyses. In the studies of Janssen *et al.* (41), Kendrick *et al.* (42) and Ringburg *et al.* (49), univariate analyses showed no significant association but multivariate analyses revealed that a higher level of SES was significantly associated with better outcome. In the study of Holbrook *et al.* (52) neither the uni- or the multivariate analyses showed a significant association. Half of the studies that used only a univariate technique found a significant association ($p<0.05$) between higher SES and better physical or psychological outcome after injury. For the studies that only used a multivariate technique, almost all studies indicated a significant association. In total, 80% of the studies found a significant assocation between a higher level of SES and better physical or psychological outcome after trauma. None of the studies reported that higher SES was significantly associated with worse outcome after non-fatal injury. See **Table 3** and **4** for more details.

Other determinants of non-fatal outcome after injury

All studies reported a wide variety of determinants of non-fatal outcome after injury. Besides SES, other demographic variables (gender, age), injury characteristics (type of injury, ISS, AIS, length of hospital stay and intensive care unit (ICU) admission), comorbidities, pre-injury working status, return to work and pain were frequently reported as significant determinants of non-fatal

Table 4: Risk of bias assessment (QUIPS)

Study	Study participation	Study attrition	Prognostic factor measurement	Outcome measurement	Study confounding	Statistical analyses and presentation
Abedzadeh-Kalahroudi *et al.* (2015) (37)	Moderate risk	High risk	High risk	Low risk	Low risk	Low risk
Attenberger *et al.* (2012) (59)	Low risk	High risk	Low risk	Low risk	Low risk	Low risk
Chiu *et al.* (2011) (47)	Low risk	High risk	Moderate risk	Low risk	Low risk	Low risk
Connelly *et al.* (2006) (40)	Low risk	Moderate risk	Moderate risk	Low risk	Low risk	Low risk
Gabbe *et al.* (2012) (38)	Low risk	Moderate risk	Low risk	Low risk	Low risk	Low risk
Glancy *et al.* (1992) (6)	Low risk	High risk	High risk	Moderate risk	Moderate risk	Moderate risk
Gross *et al.* (2011) (39)	Low risk	High risk	Moderate risk	Low risk	Low risk	Low risk
Harris *et al.* (2007, 2008) (45, 50)	Low risk	Moderate risk	Moderate risk	Moderate risk	Low risk	Low risk
Holbrook *et al.* (1998, 1999, 2001) (8, 19, 51)	Low risk	High risk	Moderate risk	Low risk	Low risk	Low risk
Holbrook *et al.* (1994) (52)	Low risk	Low risk	Moderate risk	Low risk	Moderate risk	Moderate risk
Holmes *et al.* (2010a, 2010b, 2013) (46, 57, 58)	Low risk	High risk	Moderate risk	Low risk	Low risk	Low risk
Holtslag *et al.* (2007) (4)	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Janssen *et al.* (2009) (41)	Low risk	Moderate risk	Moderate risk	Moderate risk	Moderate risk	Low risk
Kendrick *et al.* (2013) (42)	Low risk	Moderate risk	Low risk	Moderate risk	Low risk	Low risk
Langley *et al.* (2011) (54)	Low risk	High risk	Low risk	Low risk	Low risk	Low risk
MacKenzie *et al.* (1998) (3)	Moderate risk	High risk	Moderate risk	Moderate risk	Low risk	Low risk
Meerding *et al.* (2004) (10)	Low risk	High risk	High risk	Low risk	Low risk	Low risk
Michaels *et al.* (1998) (55)	Low risk	High risk	High risk	Low risk	Low risk	Low risk
Rainey *et al.* (2014) (44)	Low risk	High risk	Low risk	Low risk	Low risk	Low risk
Ringburg *et al.* (2011) (49)	Low risk	High risk	Moderate risk	Low risk	Low risk	Low risk
Sirois *et al.* (2009) (53)	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Sluys *et al.* (2005) (56)	Low risk	Low risk	Moderate risk	Low risk	Low risk	Low risk
Sorensen *et al.* (2008) (43)	Low risk	High risk	Moderate risk	Low risk	Low risk	Low risk
Trost *et al.* (2015) (48)	Low risk	High risk	Low risk	Low risk	Low risk	Low risk

Note: Table presents risk of bias assessment according to the Quality of Prognostic Studies (QUIPS) tool

outcome after injury. In some studies worse outcome was significantly associated with living alone, depression, alcohol dependence and smoking status whereas in other studies these asssociations were not found. See **Appendix 4.B** in Supplementary material for an overview of all determinants.

The effect of SES on other outcomes

In three studies included in the review, the role of SES was also examined in other outcomes besides the physical or psychological outcome. In the study of Sluys *et al.* (56), patients who reported fair or poor information during in-hospital acute care and/or at discharge had higher educational levels than patients that reported excellent, very good or good information. In two studies (3, 10) educational level was a significant determinant of longer absence duration and return to work.

DISCUSSION

This systematic review aimed to provide a better insight into the effect of SES on non-fatal outcome after injury. Methodologically, the majority of the included studies were of moderate quality since in most studies a high risk of bias on the item 'study attrition' was scored and a moderate risk of bias was found on the item 'prognostic factor measurement'. This review demonstrated that there were large differences in methodology to determine SES. For that reason we were not able to perform a meta-analysis. However, we conclude that SES is an important determinant of non-fatal outcome after injury since all studies included in this review found a positive association between a low SES level and lower psychological or physical outcome after injury (80% of studies significant, n=19).

There is lack of a clear definition of SES. Furthermore, we have shown that the differences in methodology to determine SES widely vary. Without an adequate definition of SES it is difficult to measure its role on outcome. Our review showed that education (alone or in combination with annual income) was used the most frequently to determine patients' SES. In line with earlier studies (63, 64), this review demonstrated that those with a low level of SES have worse physical or psychological outcome. This can be explained by the fact that educational level and income have an association with health (65, 66) meaning that both higher education level and higher income are associated with better health.

In the study of Sorenson *et al.* (43), income as an indicator of SES revealed a higher significant association with genderual dysfunction in the multiple regression analysis than education level. This result is in contrast with the study of Meerding *et al.* (10) in which multivariate analyses on outcome on the EQ-5D showed that educational level performed better than income. Our review showed that SES is a multidimensional concept. This implies that SES can not be measured adequately with one variable and this finding is in line with earlier studies (67-69).

Although various statistical methods were used, all studies concluded that a higher level of SES was associated with better physical and psychological outcome after injury. The included studies examined the effects of different determinants on non-fatal outcome. A large overlap between determinants that had a significant association with outcome after trauma was found among the included studies.

Until recently, little attention was paid to the effect of SES on non-fatal outcome after injury. The majority of the included studies in this review were published in the last ten years. The studies showed large variations in methodology; they differed in the number of participants, in time assessments of the measures and statistical analyses. The QUIPS-tool was used to determine the methodologic quality of the included studies. Overall, the methodologic quality was moderate. Almost all studies had a low risk of bias on the QUIPS-item 'study participation'. A well-known risk is selection bias occuring when patients with certain characteristics have a higher probability of being included in the study (70). Despite the good response rates, a high risk of bias was found in the majority of the studies on the item 'study attrition'. Important differences between the responders and non-responders were often not reported, there was a lack of adequate description of the lost to follow-up and there was a lack of clear reasons for the lost to follow-up. Since there is no clear definition of SES, we found a wide range of risk of bias on the item 'prognostic factor measurement'.

To our knowledge this is the first systematic review that summarized the current knowledge on the effect of SES on non-fatal outcome after injury. This review included patients with all types of injury and injury severity, leading to a complete view for the general trauma population. Clearly, our review has some limitations. First of all, the screening of all titles to determine whether studies were eligible for inclusion were conducted by one author. Second, the included studies showed a large variety in the number of included patients, outcomes, time assessments and methodological quality. Third, there was a lack of consistent measurement of SES. Fourth, in all included studies SES was one of the many variables that were assessed. Last, our review was restricted to studies that were published in peer-reviewed English language journals. In addition, there was an important limitation to the studies included in our review; several studies did not reported the cut-off points (e.g. High School) to determine patients' SES. Nonetheless, our results will contribute to the prevention of injury survivors for worse physical and psychological outcome.

Because of the multidimensionality of SES, we recommend measuring multiple variables instead of a single variable, although it is practically impossible to measure all the relevant dimensions. Researchers should acknowledge that residual confounding of SES occurs even when using multiple variables (1).

When educational level is used as a variable to determine SES, researchers should use clear cut-off points that correspond to earned educational degrees, such as High School. When income is used, researchers should keep in mind that income can fluctuate over time and income is often age-dependent. Besides, one-third of the respondents are unwilling to reveal their income (71). Household income should be used rather than indivual income, in particular for women who may not be the main earners in the household. Some authors recommend to divide patients' income by the family size to determine the income-to-needs ratio [68]. According to Mutaner *et al.* (72) wealth, measured by acquired capital (e.g. car or home ownership), is preferred in addition to income. However, wealth is extremely difficult to measure. The advantage of SES indices (e.g. Helmert Index) is that an index provides information on both social and material deprivation (71). Preferably we do not recommend the use of area-based SES. Using patients' zip code is based upon the assumption of population homogeneity. Correlations between individual-based SES (e.g. education or income) and zip code are low (73, 74) in which the lowest correlations are found in rural areas (75).

CONCLUSION

SES is an umbrella term for a range of variables and concepts. Though an adequate and valid measure of SES is still lacking, the results of this review showed that SES is an important determinant of non-fatal outcome for the general trauma population. Future research should focus on the definition and measurement of SES and should further underpin the effect of SES on non-fatal outcome after injury.

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APPENDICES

Appendix 4.A: Search terms

Literature search conducted on November 3rd, 2015

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('socioeconomics'/exp OR employment/exp OR career/de OR neighborhood/exp OR 'family size'/exp OR 'named groups by marital status'/exp OR 'social environment'/de OR 'social status'/exp OR 'urban area'/exp OR 'urban population'/exp OR city/de OR 'rural area'/exp OR 'rural population'/exp OR 'rural health care'/exp OR 'urban rural difference'/exp OR 'ethnic group'/de OR 'ethnic or racial aspects'/exp OR 'minority group'/exp OR 'social determinants of health'/de OR 'health disparity'/de OR 'health care disparity'/de OR inc/de OR salary/de OR 'salary and fringe benefit'/de OR household/de OR (socioeconomic* OR sociodemograph* OR (socio NEXT/1 (economic* OR demograph*)) OR ((education* OR residen* OR Domicil* OR famil* OR social OR living OR communit* OR household) NEAR/3 (status* OR character* OR background OR environment* OR class OR position OR condition* OR context* OR inequalit*)) OR inc* OR salary OR salaries OR povert* OR wealth* OR ((employ* OR occupation*) NEAR/3 (status OR state OR patient* OR class*)) OR (class* NEAR/3 (differen* OR inequal*)) OR employment* OR unemploy* OR career* OR neighborhood* OR neighbourhood* OR deprivation* OR deprived OR ((urban OR suburban* OR metropol* OR city OR innercity OR cities OR rural OR region* OR ethnic* OR minorit* OR race OR racial) NEAR/3 (determinant* OR differen* OR risk OR between* OR compar* OR variation*)) OR ((race OR ethnic* OR racial) NEXT/1 group) OR ((urban OR city OR cities) NEAR/3 (rural OR county OR countryside OR metropol*)) OR ((postal OR zip) NEXT/1 code*) OR (health* NEAR/3 disparit*) OR (Living NEXT/1 Standard*) OR illitera*):ab,ti) AND ('emergency patient'/de OR 'emergency health service'/exp OR 'emergency care'/exp OR 'emergency treatment'/de OR 'emergency surgery'/de OR 'emergency care'/exp OR 'emergency ward'/exp OR (((emergency OR emergencies OR injury*) NEXT/2 (patient* OR care OR 'health care' OR healthcare OR ward* OR centre* OR center* OR hospital* OR department* OR admission* OR treatment* OR surger* OR service* OR medicine OR medical OR room OR rooms OR visit* OR interact* OR interven* OR procedure* OR readmission* OR admission* OR manage* OR attend* OR respon* OR assist* OR presentation*)) OR (injury* NEXT/1 injur*) OR ((major OR medical) NEXT/1 emergenc*) OR (acute NEXT/1 (care OR 'health care' OR healthcare OR hospital*))):ab,ti) AND ('outcome assessment'/exp OR 'treatment outcome'/de OR 'treatment failure'/de OR rehabilitation/de OR 'functional assessment'/de OR 'quality of life'/exp OR 'health status'/de OR 'health status indicator'/de OR 'patient acuity'/de OR 'severity of illness index'/de OR wellbeing/de OR 'psychological well being'/de OR survival/de OR 'long term survival'/de OR 'overall survival'/de OR 'short term survival'/de OR 'survival rate'/de OR survivor/de OR lethality/de OR mortality/de OR 'daily life activity'/exp OR 'general health status assessment'/exp OR satisfaction/de OR (((recover* OR outcome* OR consequence* OR assess* OR status* OR Independen*) NEAR/3 (function* OR psycholog* OR non-fatal OR disab*)) OR ((outcome*) NEAR/3 (assess* OR measure* OR long-term OR short-term OR postdischarge OR post-discharge OR treatment* OR poor OR good)) OR (Treatment NEAR/3 (Fail* OR succes*)) OR (quality NEAR/3 life) OR hrql OR qol OR (health NEXT/1 (status OR state)) OR wellbeing OR well-being OR ((surviv* OR mortalit*) NEAR/6 (term OR rate OR overall OR odds OR differen* OR patient* OR determinant* OR inequalit* OR affect* OR predict* OR prognos*)) OR (daily NEAR/3 (life OR living) NEAR/3 activit*) OR (permanent* NEAR/3 impair*) OR ((sick* OR Patient* OR illness* OR personal*) NEAR/3 (impact* OR Acuit* OR sever* OR satisf*))):ab,ti) AND ('cohort analysis'/exp OR 'longitudinal study'/exp OR 'prospective study'/exp OR 'retrospective study'/exp OR 'multicenter study'/exp OR 'major clinical study'/de OR 'follow up'/exp OR (cohort* OR longitudinal* OR prospectiv* OR retrospectiv* OR multicent* OR (multi NEXT/1 (cent*)) OR ((select* OR compar*) NEAR/6 (hospital* OR center* OR centre* OR department*)) OR Nationwide OR 'follow up' OR followup OR (population NEAR/3 based)):ab,ti) NOT ([Conference Abstract]/lim OR [Letter]/lim OR [Note]/lim OR [Editorial]/lim)

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(exp "Socioeconomic Factors"/ OR employment/ OR Unemployment/ OR "Residence Characteristics"/ OR "Family Characteristics"/ OR exp "Marital Status"/ OR "social environment"/ OR "urban population"/ OR "Urban Health"/

OR “Urban Health Services”/ OR “Suburban Population”/ OR cities/ OR “Rural Population”/ OR “Rural Health”/ OR “Rural Health Services”/ OR “ethnic groups”/ OR “Minority Groups”/ OR “Minority Health”/ OR “Social Determinants of Health”/ OR “Health Status Disparities”/ OR “Healthcare Disparities”/ OR inc/ OR “Salaries and Fringe Benefits”/ OR (socioeconomic* OR sociodemograph* OR (socio ADJ (economic* OR demograph*)) OR ((education* OR residen* OR Domicil* OR famil* OR social OR living OR communit* OR household) ADJ3 (status* OR character* OR background OR environment* OR class OR position OR condition* OR context* OR inequalit*)) OR inc* OR salary OR salaries OR povert* OR wealth* OR ((employ* OR occupation*) ADJ3 (status OR state OR patient* OR class*)) OR (class* ADJ3 (differen* OR inequal*)) OR employment* OR unemploy* OR career* OR neighborhood* OR neighbourhood* OR deprivation* OR deprived OR ((urban OR suburban* OR metropol* OR city OR innercity OR cities OR rural OR region* OR ethnic* OR minorit* OR race OR racial) ADJ3 (determinant* OR differen* OR risk OR between* OR compar* OR variation*)) OR ((race OR ethnic* OR racial) ADJ group) OR ((urban OR city OR cities) ADJ3 (rural OR county OR countryside OR metropol*)) OR ((postal OR zip) ADJ code*) OR (health* ADJ3 disparit*) OR (Living ADJ Standard*) OR illitera*).ab,ti.) AND (“Emergency Medicine”/ OR exp “Emergency Medical Services”/ OR “Emergency Treatment”/ OR (((emergency OR emergencies OR injury*) ADJ (patient* OR care OR “health care” OR healthcare OR ward* OR centre* OR center* OR hospital* OR department* OR admission* OR treatment* OR surger* OR service* OR medicine OR medical OR room OR rooms OR visit* OR interact* OR interven* OR procedure* OR readmission* OR admission* OR manage* OR attend* OR respon* OR assist* OR presentation*)) OR (injury* ADJ injur*) OR ((major OR medical) ADJ emergenc*) OR (acute ADJ3 (care OR healthcare OR hospital*))).ab,ti.) AND (“Outcome Assessment (Health Care)”/ OR “Patient Outcome Assessment”/ OR “Treatment Outcome”/ OR “Treatment Failure”/ OR Rehabilitation/ OR Rehabilitation.xs. OR “Quality of Life”/ OR “Health Status”/ OR “Health Status Indicators”/ OR exp “Patient Acuity”/ OR “Sickness Impact Profile”/ OR “Personal Satisfaction”/ OR survival/ OR survivors/ OR mortality/ OR mortality.xs. OR “Activities of Daily Living”/ OR (((recover* OR outcome* OR consequence* OR assess* OR status* OR Independen*) ADJ3 (function* OR psycholog* OR non-fatal OR disab*)) OR ((outcome*) ADJ3 (assess* OR measure* OR long-term OR short-term OR postdischarge OR post-discharge OR treatment* OR poor OR good)) OR (Treatment ADJ3 (Fail* OR succes*)) OR (quality ADJ3 life) OR hrql OR qol OR (health ADJ (status OR state)) OR wellbeing OR well-being OR ((surviv* OR mortalit*) ADJ6 (term OR rate OR overall OR odds OR differen* OR patient* OR determinant* OR inequalit* OR affect* OR predict* OR prognos*)) OR (daily ADJ3 (life OR living) ADJ3 activit*) OR (permanent* ADJ3 impair*) OR ((sick* OR Patient* OR illness* OR Personal*) ADJ3 (impact* OR Acuit* OR sever* OR Satisf*))).ab,ti.) AND (exp “cohort studies”/ OR “multicenter study”/ OR (cohort* OR longitudinal* OR prospectiv* OR retrospectiv* OR multicent* OR (multi ADJ (cent*)) OR ((select* OR compar*) ADJ6 (hospital* OR center* OR centre* OR department*)) OR Nationwide OR “follow up” OR followup OR (population ADJ3 based)).ab,ti.) NOT (letter OR news OR comment OR editorial OR congresses OR abstracts).pt.

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((socioeconomic* OR sociodemograph* OR (socio NEXT/1 (economic* OR demograph*)) OR ((education* OR residen* OR Domicil* OR famil* OR social OR living OR communit* OR household) NEAR/3 (status* OR character* OR background OR environment* OR class OR position OR condition* OR context* OR inequalit*)) OR inc* OR salary OR salaries OR povert* OR wealth* OR ((employ* OR occupation*) NEAR/3 (status OR state OR patient* OR class*)) OR (class* NEAR/3 (differen* OR inequal*)) OR employment* OR unemploy* OR career* OR neighborhood* OR neighbourhood* OR deprivation* OR deprived OR ((urban OR suburban* OR metropol* OR city OR innercity OR cities OR rural OR region* OR ethnic* OR minorit* OR race OR racial) NEAR/3 (determinant* OR differen* OR risk OR between* OR compar* OR variation*)) OR ((race OR ethnic* OR racial) NEXT/1 group) OR ((urban OR city OR cities) NEAR/3 (rural OR county OR countryside OR metropol*)) OR ((postal OR zip) NEXT/1 code*) OR (health* NEAR/3 disparit*) OR (Living NEXT/1 Standard*) OR illitera*):ab,ti) AND ((((emergency OR emergencies OR injury*) NEXT/2 (patient* OR care OR ‘health care’ OR healthcare OR ward* OR centre* OR center* OR hospital* OR department* OR admission* OR treatment* OR surger* OR service* OR medicine OR medical OR room OR rooms OR visit* OR interact* OR interven* OR procedure* OR readmission* OR admission* OR manage* OR attend* OR respon* OR assist* OR presentation*)) OR (injury* NEXT/1 injur*) OR ((major OR medical) NEXT/1 emergenc*) OR (acute NEXT/1 (care OR ‘health care’ OR healthcare OR hospital*))):ab,ti) AND ((((recover* OR outcome* OR consequence* OR assess* OR status* OR Independen*) NEAR/3 (function* OR psycholog* OR non-fatal OR disab*)) OR ((outcome*) NEAR/3 (assess* OR measure* OR long-term OR short-term OR postdischarge OR post-discharge OR treatment* OR poor OR good)) OR (Treatment NEAR/3 (Fail* OR succes*)) OR (quality NEAR/3 life) OR hrql OR qol OR (health NEXT/1 (status OR state)) OR wellbeing OR well-being OR ((surviv* OR mortalit*) NEAR/6 (term OR rate OR overall OR odds OR differen* OR patient* OR determinant* OR inequalit* OR affect* OR predict* OR prognos*)) OR (daily NEAR/3 (life OR living) NEAR/3 activit*) OR (permanent* NEAR/3 impair*) OR ((sick* OR Patient* OR illness* OR personal*) NEAR/3 (impact* OR Acuit* OR sever* OR satisf*))):ab,ti) AND ((cohort* OR longitudinal* OR prospectiv* OR retrospectiv* OR multicent* OR (multi NEXT/1 (cent*)) OR ((select* OR compar*) NEAR/6 (hospital* OR center* OR centre* OR department*)) OR Nationwide OR ‘follow up’ OR followup OR (population NEAR/3 based)):ab,ti)

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TS=(((socioeconomic* OR sociodemograph* OR (socio NEAR/1 (economic* OR demograph*)) OR ((education* OR residen* OR Domicil* OR famil* OR social OR living OR communit* OR household) NEAR/2 (status* OR character* OR background OR environment* OR class OR position OR condition* OR context* OR inequalit*)) OR inc* OR salary OR salaries OR povert* OR wealth* OR ((employ* OR occupation*) NEAR/2 (status OR state OR patient* OR

class*)) OR (class* NEAR/2 (differen* OR inequal*)) OR employment* OR unemploy* OR career* OR neighborhood* OR neighbourhood* OR deprivation* OR deprived OR ((urban OR suburban* OR metropol* OR city OR innercity OR cities OR rural OR region* OR ethnic* OR minorit* OR race OR racial) NEAR/2 (determinant* OR differen* OR risk OR between* OR compar* OR variation*)) OR ((race OR ethnic* OR racial) NEAR/1 group) OR ((urban OR city OR cities) NEAR/2 (rural OR county OR countryside OR metropol*)) OR ((postal OR zip) NEAR/1 code*) OR (health* NEAR/2 disparit*) OR (Living NEAR/1 Standard*) OR illitera*)) AND ((((emergency OR emergencies OR injury*) NEAR/2 (patient* OR care OR "health care" OR healthcare OR ward* OR centre* OR center* OR hospital* OR department* OR admission* OR treatment* OR surger* OR service* OR medicine OR medical OR room OR rooms OR visit* OR interact* OR interven* OR procedure* OR readmission* OR admission* OR manage* OR attend* OR respon* OR assist* OR presentation*)) OR (injury* NEAR/1 injur*) OR ((major OR medical) NEAR/1 emergenc*)) OR (acute NEAR/1 (care OR 'health care' OR healthcare OR hospital*))) AND ((((recover* OR outcome* OR consequence* OR assess* OR status* OR Independen*) NEAR/1 (function* OR psycholog* OR non-fatal OR disab*)) OR ((outcome*) NEAR/2 (assess* OR measure* OR long-term OR short-term OR postdischarge OR post-discharge OR treatment* OR poor OR good)) OR (Treatment NEAR/2 (Fail* OR succes*)) OR (quality NEAR/2 life) OR hrql OR qol OR (health NEAR/1 (status OR state)) OR wellbeing OR well-being OR ((surviv* OR mortalit*) NEAR/5 (term OR rate OR overall OR odds OR differen* OR patient* OR determinant* OR inequalit* OR affect* OR predict* OR prognos*)) OR (daily NEAR/2 (life OR living) NEAR/2 activit*) OR (permanent* NEAR/2 impair*) OR ((sick* OR Patient* OR illness* OR personal*) NEAR/2 (impact* OR Acuit* OR sever* OR satisf*))))) AND ((cohort* OR longitudinal* OR prospectiv* OR retrospectiv* OR multicent* OR (multi NEAR/1 (cent*)) OR ((select* OR compar*) NEAR/5 (hospital* OR center* OR centre* OR department*)) OR Nationwide OR "follow up" OR followup OR (population NEAR/3 based)))) AND DT=(article)

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Appendix 4.B: Other determinants of physical or psychological outcome after non-fatal injury

Author, year	Correction determinants in multivariate analyses	Determinants
Abedzadeh-Kalahroudi *et al.* (2015) (37)	**Demogr:** age*, gender. **Injury:** ISS*, no. of injured organ, injury type, no. of surgery, LOS*, ICU admission, extremity injury*	**Demogr:** age*, gender, nationality. **Injury:** injury severity*, ICU transfer*, injury type*. **Extra:** RTW*
Attenberger *et al.* (2012) (59)	n.a.	**Demogr:** Swiss*. **Injury:** SAPS II mortality*, NTDB-TRISS, time to operation room intervention within 6h following hospital arrival*, LEP (mean nurse workload per day and patient)*, change of type of work due to injury*, reduced working capacity due to injury*, court case due to injury*, daily allowance due to injury*, decrease of income due to injury*. **Extra:** smoking pre-injury*, EQ-5D*, SF-36*, MFA*, FIM*, GOS*, ALOS*, NHP*, well-being at time of FU*, change of life*
Chiu *et al.* (2011) (47)	**Demogr:** marital status, age. **Injury:** injury type*	**Demogr:** age*, ethnicity*, employment*, marital status*, gender. **Injury:** (non-)assaultive injury type*, ISS, GCS at scene
Connelly *et al.* (2006) (40)	**Demogr:** age, marital status*. **Injury:** ISS*, GCS*, type of injury , Neurosurgery unit*, ICU stay*, total stay*, transferred, visit GP or hospital clinic, visit therapist, compensation, PTSD. **Extra:** consulting psych prior to injury, manual work, pre-work*, smoking, alcohol	n.a.
Gabbe *et al.* (2012) (38)	**Demogr:** age*, gender*. **Injury:** mechanism*, intent of injury*, head injury severity*, injury group*, definitive management*. **Extra:** comorbidity*, year injured*, pre-injury disability*, employment status, compensable status*	**Demogr:** age*, gender*. **Injury:** mechanism*, intent of injury*, head injury severity*, injury group*, definitive management*. **Extra:** comorbidity*, year injured*, pre-injury disability*, employment status*, compensable status
Glancy *et al.* (1992) (6)	Age* and ISS* **Other testing variables, corrected for age and ISS:** **Demogr:** household type*, marital status. **Injury:** previous trauma, work related injury. **Extra:** disability inc as a percentage of pre-injury*, litigation*, SCL-90-R (psychological symptom patterns)*, health insurance, disability insurance, workman's compensation, self-employed, decreased activity, MSPSSS total score	n.a.
Gross *et al.* (2011) (39)	**Injury:** greater AIS V*, TBI, higher TRISS. **Extra:** greater BMI, blue collar*, more pain pre*, lesser EQ-5D pre*	n.a.

Appendix 4.B *(continued)*

Author, year	Correction determinants in multivariate analyses	Determinants
Harris *et al.* (2007,2008) (45, 50)	**2007: Demogr:** comorbidity*. **Injury:** mechanism*. **Extra:** claim* **2008: Demogr:** chronic illnesses, age*. **Injury:** time since injury*, ISS*, head injury*. **Extra:** claim*, lawyer used*	**2007: Demogr:** age, gender, comorbidity*. **Injury**: time since injury*, injury mechanism*, ISS, ICU admission, head injury. **Extra:** employment, claim-related factors **2008: Demogr:** age*, gender*. **Injury:** time since injury*, ISS*, ICU days*, head injury*. **Extra**: chronic illnesses*, claim related factors*, ICU admission
Holbrook *et al.* (1998, 1999, 2001) (8, 19, 51)	**1998: Demogr:** gender*, age*. **Injury:** ICU days*, LOS*, major injury to extremities (AIS 3+)*, ISS. **Extra:** social satisfaction, depression at discharge, depression at 6mo. FU*, IES-A and IES-I score* **1999: Demogr:** age*	**2001: Demogr:** age*, marital status. **Injury:** AIS (head, chest, abdomen and extremities), RTS, ISS, ICU days, LOS **1999: Demographic:** marital status*, gender. **Injury:** serious extremity (AIS 3+)*. **Extra:** depression at discharge, 6 or 12mo*, depression-discharge through 6mo or 12mo*, IES-I high vs low*, social support
Holbrook *et al.* (1994) (52)	**Model 1: Demogr:** age, gender, race, marital status. **Extra:** % change in QWB: CES-D pre-discharge*, social support, satisfaction, drinking, drug, mental problems. **Model 3: Demogr:** age, CES-D pre-discharge*, gender, race, marital status. **Extra:** social support, satisfaction, drinking, drug, mental problem	**Demogr:** Gender, marital status, race. **Injury:** injury type, operation, major complication. **Extra:** depression*, social support
Holmes *et al.* (2010a, 2010b, 2013) (46, 57, 58)**	**Injury:** Injury severity*. **Extra:** initial current pain*	**Demogr:** age, gender, marital status, children, living status*, current work*. **Injury:** context, cause, severity*, site*, injury care*. **Extra:** health-related function*, mental health*, psychiatric disorder, depression*, anxiety*, anger*, alcohol dependence*, alcohol abuse, substance dependence, pain*, pain management*, social support, pain cognitions*, surgery*
Holtslag *et al.* (2007) (4)	**Model A: Demogr:** gender, age, household. **Injury:** severity. **Extra:** BMI, comorbidity*. **All other models: Demogr:** gender*, age, household. **Injury:** injury severity, injury localization*. **Extra:** BMI, comorbidity*	**Demogr:** age*, gender*, household composition*. **Injury:** severity, injury location*. **Extra:** BMI*, comorbidity*
Janssen *et al.* (2009) (41)	**Step 1: Demogr:** age*, gender. **Additional variables: Step 2: Injury:** injury severity, injury of extremities. **Extra:** subjective evaluation of medical treatment outcome*, time after discharge, behavioural intervention, shared decision making*	**Demogr:** age, gender. **Injury:** injury severity, injury of extremities. **Extra:** subjective evaluation of medical treatment outcome*, time after discharge, behavioural intervention, shared decision making*
Kendrick *et al.* (2013) (42)	n.a.	**Demogr:** gender*, age*, ethnicity. **Injury:** admission status*, injury severity*, body region injured*, place of injury*, injury intent. **Extra**: long-term illness, study centre*, living alone

Appendix 4.B *(continued)*

Author, year	Correction determinants in multivariate analyses	Determinants
Langley *et al.* (2011) (54)	**Corrected for: Demogr:** gender*, age*. **Injury:** body region*, nature of injury*, intent*, admission*. **Extra:** disability comorbidity*, overall health*, obese, depressed*, smoking*, alcohol inactivity*, self-perceived threat to life and disability*, healthcare services*	**Demogr:** gender, age. **Injury:** injuries multiple body regions, nature of injury, intent of injury, hospitalization**. Extra:** living arrangements, working for pay, self-perceived threat to life or disability, difficulty accessing health services, chronic illness, disability, overall health, BMI, optimistic, general self-efficacy, depressed, spiritual beliefs, smoking, alcohol, drugs, activity, admission to hospital
MacKenzie *et al.* (1988) (3)	n.a.	n.a.
Meerding *et al.* (2004) (10)	**Demogr:** age*, gender*. **Injury:** hospital LOS*, type of injury*, motor vehicle involvement*, no. of injuries, medical operation, admission ICU*	n.a.
Michaels *et al.* (1998) (55)	n.a.	**Demogr:** age*, gender, regular religious practice*. **Injury:** ISS. **Extra:** Acute Stress Disorder*, work status, psychosocial status, IES score*, peri-traumatic dissociation*
Rainey *et al.* (2014) (44)	n.a.	**Extra**: employment*
Ringburg *et al.* (2011) (49)	**Demogr:** gender*, age, living alone*. **Injury:** ISS*, injury localization*. **Extra:** comorbidity*, helicopter emergency medical services	**Demogr:** gender*, age*, household composition*, living alone. **Injury**: ISS*, injury localization. **Extra**: comorbidity*, type of pre-hospital care
Sirois *et al.* (2009) (53)	**Demogr**: age*, gender*, marital status. **Injury**: ISS, acute care complications*, time since injury. **Extra**: social support*, provincial automobile insurances*, active employment*, comorbidities*	n.a.
Sluys *et al.* (2005) (56)	n.a	**Demogr**: gender, marital status*. **Injury:** type of injury*, mechanism of blunt injury, major inhospital complication*, acute in-hospital care*, ICU admission >5 days*, ISS*, NISS*, injury localization*. **Extra:** physical injury, admission to rehabilitation*, insufficient care from hospital*
Sorensen *et al.* (2008) (43)	**Corrected for: Demogr:** age*. **Injury:** ISS*, specific injury patterns*. **Extra:** global self-reported health*, pre-existing diabetes*	**Demogr**: age*, gender, ethnicity, marital status*. **Injury:** ISS*, maximal AIS*, mechanism of injury, other markers of injury severity*, specific injury patterns*. **Extra:** baseline global health status*, comorbidity*
Trost *et al.* (2015) (48)	**Corrected for: Demogr:** age*. **Injury:** trauma type. **Extra:** Injustice Experiences Questionnaire*, pain, veterans RAND survey MCS*	n.a.

Legend of **Appendix 4.B**

*significant

**not representing a complete generic injury population

Abbreviations: AIS, Abbreviated Injury Scale; ALOS, Aachen Long–term Outcome Score; BMI, body mass index; demogr, demographic; EQ–5D, EuroQol five dimensions questionnaire; FIM, Functional Independence Measure; FU, follow–up; GCS, Glasgow Coma Scale; GOS, Glasgow Outcome Scale; GP, general practitioner; ICD–9, International Classification of Diseases–9; ICU, intensive care unit; IES, Impact of Event Scale; ISS, Injury Severity Score; LOS, length of stay; MCS, mental component score; MFA, Musculoskeletal Functional Assessment; mo., month; n.a., not applicable; NHP, Notthingham Health Profile; NTDB–TRISS, National Trauma Data Bank–Trauma and Injury Severity Score; PTSD, post–traumatic stress disorder; QWB, Quality of well–being scale; RTS, Revised Trauma Score; RTW, return to work; SAPS II mortality, Simplified Acute Physiology Score II mortality; SF–36, Short Form–36; TBI, traumatic brain injury; TRISS, Trauma and Injury Severity Score; Veterans RAND–12, Veterans Research and Development–12.

5

Chapter

Comparison of pre-injury recalled Health Status (HS) data of trauma patients and HS of the gereral population

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Injury 2019;**50**(4):890-897
DOI 10.1016/j.injury.2019.03.039

ABSTRACT

Purpose: Significant differences exist between retrospectively collected pre-injury Health Status (HS) of trauma patients and the HS of the general population. Compared to the general population, the trauma population includes a larger proportion of individuals with a low level of socio-economic status. The aim was to compare retrospectively collected pre-injury HS with HS of a sample of Dutch individuals not only adjusted for age and gender, but also for educational level.

Methods: Within three months post-trauma, pre-injury HS (n=2,987) was collected by using the EuroQol-five-dimension-3-level (EQ-5D-3L) questionnaire. Data were abstracted from the Brabant Injury Outcome Surveillance. The reference cohort (n=1,839) included a sample of the Dutch general population. Multiple regression was used to compare HS of both cohorts.

Results: A higher recalled pre-injury EQ-5D-3L score of the injury cohort was reported compared to the HS of the reference cohort after adjustment for age (β=0.014 [95% CI: 0.001,0.027] for males and β=0.018 [95% CI: -0.001, 0.036] for females). After adjustment for age and educational level, the Beta showed a ≥10% increasement: males; unadjusted β=0.006 [95% CI: -0.007, 0.019] to β=0.014 [95% CI: 0.001, 0.027] after age adjustment to β=0.020 [95% CI: 0.007, 0.033] after adjustment for age and educational level, females; unadjusted β=-0.018 [95% CI: -0.035, -0.001] to β=0.018 [95% CI: -0.001, 0.036] after age adjustments to β=0.025 [95% CI: 0.007, 0.043] after adjustments for age and educational level. After adjustment for age, gender and educational level, the injury cohort reported prior to the trauma less problems on the 'pain/discomfort' (OR=0.522 [95% CI: 0.454, 0.602]) and the 'anxiety/depression' (OR=0.745 [95% CI: 0.619, 0.897]) dimensions, as compared to the reference cohort. In contrast, the injury cohort reported significantly more problems on the 'self-care' dimension (OR=1.497 [95% CI: 0.1.112, 2.016]) prior to the trauma.

Conclusions: Injured patients report better recalled pre-injury HS compared to the HS of the reference cohort. After adjustment for educational level, the difference in HS between the injury cohort and the reference cohort increases, underlining that other confounders might also influence HS.

Trail registration: ClinicalTrials.gov identifier: NCT02508675.

Keywords: injury, trauma, pre-injury status, health status, retrospective measurement, educational level.

BACKGROUND

To produce valid estimates of the health impact and the decrease of functioning after trauma, information on patients functioning prior to the trauma is crucial (1-4). For instance, pre-existing disability is highly related to problems with mobility and pain post-trauma (5). Therefore, knowledge about the change from pre-injury to post-injury Health Status (HS) is important in order to derive population estimates of the impact of a trauma (6). However, insight into this change requires a HS norm. In trauma research there are two dominant approaches to assess the HS norm that is used to measure change in HS.

The first approach uses pre-injury HS as a norm. In this approach pre-injury HS is mostly assessed retrospectively, even though it is well-known that retrospectively collected data can be distorted due to recall bias or response shift (6). Recall bias appears when people remember their former state as better or worse than it actually was (7). Response shift occurs when, aggravated by a life event such as a trauma, people do not maintain a consistent internal scale for their responses over time (8). Subsequently, patients' perception of HS might change after a trauma (9). Both recall bias and response shift are presumed to lead to a systematic overestimation of the HS prior to the trauma (6).

In the second approach, HS of the general population is used as a norm to measure change in HS (10-13). An advantage of this approach is that it is fairly easy to obtain general population norms by country, age and gender category. However, the question is if HS of the general population is representative of the pre-injury HS of the trauma population. Several studies found significant differences between retrospectively collected pre-injury HS data of trauma patients and the HS of the general population, even after adjustment for age and gender (6, 12, 14-17). Trauma patients tend to be less healthy compared to the general population (6) implying that the trauma population is not a representative sample of the general population.

An explanation for this finding may be that, compared to the general population, the trauma population includes a larger proportion of individuals with a low level of socio-economic status (SES) (e.g. educational level) (1, 18) and SES in its turn is highly associated with HS (19). For example, high educational level is associated with lower levels of emotional distress (e.g. depression, anxiety or anger), lower physical distress (e.g. pain) and a lower prevalence of comorbid conditions (19). As far as we known, no study has been conducted comparing retrospectively assessed pre-injury HS and HS of the general population after adjustment for age, gender and SES. Therefore, The aim was to compare retrospectively collected pre-injury HS with HS of a sample of Dutch individuals not only stratified by age and gender, but also by educational level.

MATERIALS AND METHODS

Design and setting

A comparative study was conducted including a cohort of injured patients and a sample of Dutch individuals adjusted for age, gender and educational level that functioned as a reference cohort.

Participants

Injury cohort

For the injury cohort, data was used from the Brabant Injury Outcome Surveillance (BIOS). The BIOS was approved by the Medical Ethics Committee Brabant, the Netherlands (project number NL50258.028.14). The study protocol is published elsewhere (20). The BIOS is a large prospective observational follow-up cohort study in which HS, psychosocial, functional outcome and costs after trauma will be assessed during two years of follow-up. The BIOS was conducted in all ten hospitals of the Dutch Noord-Brabant region.

In the BIOS, adult injured patients aged 18 and older who were admitted to an Intensive Care Unit or a ward after presentation on the emergency department (ED), and who survived to hospital discharge were eligible for inclusion. All types of trauma were included, regardless of the intent or severity. Patients were included between August 2015 and November 2016. Patients with a pathological fracture, insufficient knowledge of the Dutch language or with no permanent address of residence were excluded. For eligible patients it was possible to enter in the study at different time points, i.e. one week (T1), one month (T2), three months (T3), six months (T4) or one year (T5) post-trauma. For this study, a sub cohort of the BIOS was used (see **Figure 1**). To minimise recall bias, we used pre-injury HS data that was completed within three months post-trauma. Questionnaires completed by proxy informants were excluded. All patients gave informed consent prior to participation. Patients did not receive compensation for participation.

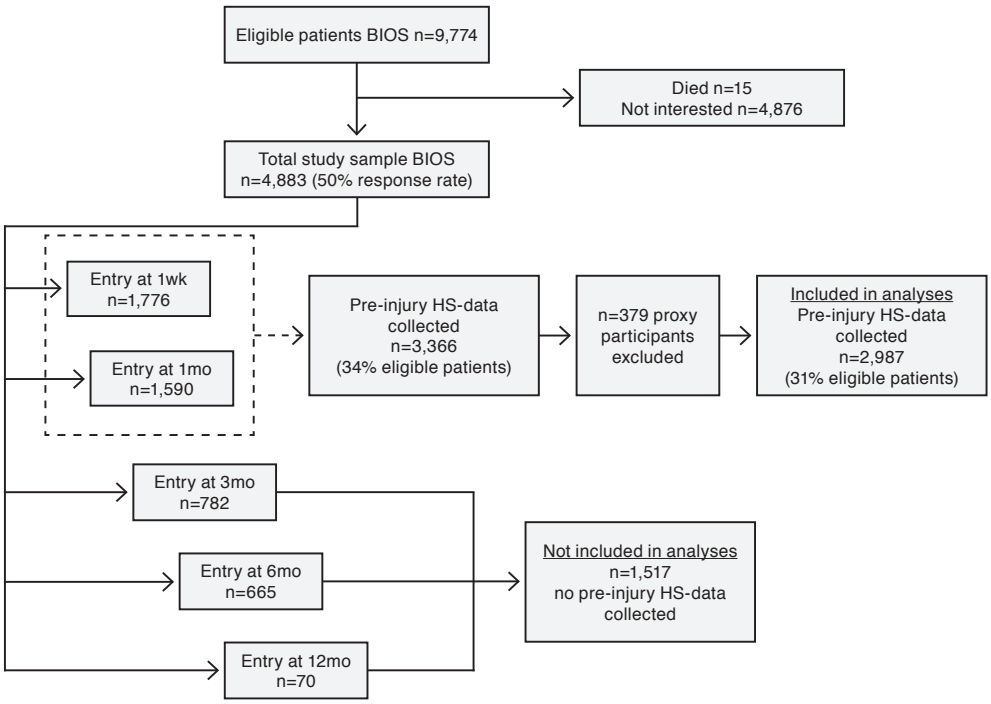

Figure 1: Flow chart of patient inclusion throughout the Brabant Injury Outcome Surveillance
Abbreviations: BIOS, Brabant Injury Outcome Surveillence; HS, Health status; mo, month(s); wk, week.

Reference cohort

Retrospectively collected pre-injury HS was compared with HS of a reference cohort. For the reference cohort, we made use of the data of the Longitudinal Internet Studies for the Social sciences (LISS) panel administered by CentERdata (Tilburg University, the Netherlands). The LISS-panel is a representative sample of the Dutch population who participate in monthly internet surveys. This panel is based on a true probability sample of households drawn from the population register (21). For the composition of the reference cohort, similar gender and age distributions as presented in the Dutch trauma population (22) were used. The trauma population is an ageing population. Therefore, we oversampled patients aged 65 or older in the LISS-panel. Since younger people generally show low inclusion rates in surveys, younger participants were oversampled as well to increase the response rate. Participants completed the HS-data in January 2016 and received an incentive for completing the questionnaire.

Educational level

Educational level as collected in the injury and reference cohort was subdivided into low, middle or high as suggested by Statistics Netherlands (23). Participants with no diploma, primary education or preparatory secondary vocational education were considered to have a low educational level. Middle educational level included participants who completed university preparatory education, senior general secondary education or senior secondary vocational education and training. Participants who completed university of applied science (associate degree) or an academic degree were considered to have high educational level.

Data collection

Demographic characteristics of the injury and reference cohort were extracted from the self-reported questionnaire and included age, gender and educational level (i.e. degree, diploma or certificate of highest education).

Outcome measures

To determine (pre-injury) HS, the EuroQol-five-dimension-3-level (EQ-5D-3L) (24) was completed by all participants. The EQ-5D-3L is a self-reported questionnaire and consists of five questions and the EuroQol Visual Analogue Scale (EQ-VAS). In the EQ-5D-3L, health is defined along five domains: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each item can be scored as ‘no problems’, ‘moderate problems’ or ‘severe problems’. For the injury cohort, the recall period of the EQ-5D-3L was one day prior to the injury, for the reference cohort the recall period was ‘today’. From the individual dimensions, a scoring algorithm can be calculated by which each health status description can be formatted into a summary score. This summary score ranges from 0 for death and 1 for full health (24). The EQ-VAS records participant’s self-rated health on a vertical visual analogue scale with two endpoints, i.e. ‘the best health you can imagine’ (score 100) and ‘the worst health you can imagine’ (score 0) (24).

Data analysis

All analyses were conducted using SPSS V.24 (Statistical Package for Social Sciences, Chicago, Illinois, USA). Statistical test results were considered significant at a level of $p<0.05$. Categorical variables were presented as frequencies (percentages), and continuous variables as mean with standard deviation (SD) or median with 25th and 75th percentiles, as appropriate.

The injury and reference cohort were stratified by age, gender and educational level. For this, six age categories (i.e. 18-34, 35-44, 45-54, 55-64 65-74 and 75 years or older) were created. Descriptive statistics were used to compare the different strata.

For the injury and reference cohort, multiple linear regression analyses were used to explain the relationship between (pre-injury) HS and age, gender and educational level (low educational level as reference group) for both the EQ-5D-3L summary score and the EQ-VAS.

For the regression analyses of the EQ-5D-3L summary score and the EQ-VAS, variables were divided into three blocks. To compare the injury and reference cohort, type of cohort was entered in block 1 (i.e. unadjusted model). In block 2, adjustments were made for age. In block 3, educational level was added to the variable of block 2. Age was entered as a continuous variable and educational level was entered as a dummy variable. Data were presented with unstandardized Beta's (β's) and the 95% Confidence Intervals (95% CI's), representing the difference in HS in the injury cohort relative to the reference cohort.

Logistic regression analyses were performed in which score options of each dimension of the EQ-5D-3L were dichotomized into 0='no problems', and 1='moderate problems'/'severe problems'. Here, no statistically significant interaction terms were identified between gender and educational level (low educational level as reference group) (mobility p-value=0.995 (for middle educational level) and p-value=0.735 (for high educational level), self-care p-value=0.387 (for middle educational level) and p-value=0.601 (for high educational level), daily activities p-value=0.992 (for middle educational level) and p-value=0.189 (for high educational level), pain/discomfort p-value=0.876 (for middle educational level) and p-value=0.076 (for high educational level), anxiety p-value=0.806 (for middle educational level) and p-value=0.609 (for high educational level)). Variables were divided into three blocks. Type of cohort was entered in block 1 (i.e. unadjusted model). In block 2, adjustments were made for gender and age. In block 3, educational level was added to the variables of block 2. For the logistic regression, Beta's, Odds Ratio's (ORs) and 95% CI's were reported.

Besides the comparison of the injury and reference cohort, we examined the confounding effect of educational level on the (pre-injury) EQ-5D-3L summary score and EQ-VAS. If the Beta changes ≥10% after adjustment for educational level in the regression analyses, educational level was considered to be a confounding variable (25).

RESULTS

General characteristics of the participants

Injury cohort – During the study period, 9,774 patients were eligible for the BIOS (see **Figure 1**). In total, 4,883 (50% response rate) participated in the BIOS of which 2,987 (31% of all eligible patients) completed the pre-injury HS-data within three months post-trauma. The median time of completing the pre-injury HS was 11 days (interquartile range 6-30). Comparisons of responders and non-responders showed that the group of responders included a larger proportion of males (46% vs 53%) and that responders were younger compared to the non-responders (mean 62 years vs 66 years). Regarding to the injuy-related characteristics, responders were more likely to have a traffic accident, a work-related injury or a sport injury. Responders were less likely to have a self-inflicted injury. Furthermore, responders with an Injury Severity Score (ISS) of 4-8 or

≥16 showed the highest response rate (36.8% and 34.0%, respectively) whereas those with an ISS 9-15 showed the lowest response rate (28.6%). Participants who were admitted ≤2 days or 3-7 days showed the highest response rate (31.9% and 34.7%, respectively) compared to those with 8-14 or ≥15 days of hospitalization (25.6% and 19.8%, respectively). In total, 33.2% of the patients that were admitted to an Intensive Care Unit participated into the study (see **Table 1**).

Reference cohort – For the reference cohort, 2,262 participants were invited of whom 1839 participated (response rate 81.3%). Comparison of responders and non-responders showed that responders were older (mean 51 years vs. 39 years) (see **Table 1**).

The injury cohort included a higher percentage of males (53% vs. 47%), and patients had a higher mean age (62 years vs. 51 years) compared to participants of the reference cohort. The responders of the reference cohort showed almost similar distributions of educational level compared to the inhabitants of the Noord-Brabant region (26) and compared to the Dutch population (27) (low education: reference cohort=27%, Noord-Brabant region=35%, Dutch population=31%; middle education reference cohort=37%, Noord-Brabant region= 41%, Dutch population=39%; high educational level: reference cohort=34%, Noord-Brabant region=24%, Dutch population=28%). Furthermore, in the injury cohort, almost half of the patients (47%) had low educational level while in the reference cohort, only 27% had low educational level (see **Table 1**).

Table 1: Demographic and injury–related characteristics of the responders and non–responders of the injury cohort and demographic characteristics of the reference cohort

	Injury cohort		Reference cohort	
	Responders (n=2,987)	Non-responders (n=6,787)	Responders (n=1,839)	Non-responders (n=423)
Males	n=1,593 (53%)	n=3,143 (46%)	n=859 (47%)	n=175 (41%)
Mean age (yrs.)	62 (SD 18)	66 (SD 22)	51 (SD 19)	39 (SD 18)
18-24	n=133 (4.5%)	n=484 (7.1%)	n=227 (12%)	n=105 (25%)
25-44	n=383 (12.8%)	n=900 (13.3%)	n=502 (27%)	n=181 (43%)
45-64	n=1,011 (33.8%)	n=1,359 (20%)	n=465 (25%)	n=82 (19%)
65-74	n=659 (22.1%)	n=867 (12.8%)	n=457 (25%)	n=30 (7.1%)
75-84	n=548 (18.3%)	n=1,584 (23.3%)	n=160 (9%)	n=21 (5%)
85+	n=253 (8.5%)	n=1,593 (23.5%)	n=28 (1.5%)	n=4 (1%)
Educational level[$]				
Low educational level	n=1,389 (47%)	n.a.[*]	n=494 (27%)	n=92 (22%)
Middle educational level	n=870 (29%)	n.a.[*]	n=677 (37%)	n=168 (40%)
High educational level	n=642 (22%)	n.a.[*]	n=623 (34%)	n=153 (36%)
Other	n=0 (0%)	n.a.[*]	n=45 (2%)	n=10 (2.4%)
Missing	n=86 (3.0%)	n.a.[*]	n=0 (0.0%)	n=0 (0%)
Cause of injury				
At home	n= 1,609 (53.9%)	n=3,808 (56.1%)	n.a.	n.a.
Traffic accident	n=866 (29.0%)	n=1,267 (18.7%)	n.a.	n.a.

Table 1 *(continued)*

	Injury cohort		Reference cohort	
	Responders (n=2,987)	Non-responders (n=6,787)	Responders (n=1,839)	Non-responders (n=423)
Work-related	n=147 (4.9%)	n=190 (2.8%)	n.a.	n.a.
Sport	n=238 (8.0%)	n=230 (3.4%)	n.a.	n.a.
Violence	n=39 (1.3%)	n=166 (2.4%)	n.a.	n.a.
Self-inflicted	n=9 (0.3%)	n=30 (0.4%)	n.a.	n.a.
Other	n=31 (0.9%)	n=51 (0.8%)	n.a.	n.a.
Missing	n=48 (1.6%)	n=1,045 (15.4%)	n.a.	n.a.
Mean ISS				
1-3	n=751 (25.1%)	n=1,754 (25.8%)	n.a.	n.a.
4-8	n=1,072 (35.9%)	n=1,845 (27.2%)	n.a.	n.a.
9-15	n=995 (33.3%)	n=2,489 (36.7%)	n.a.	n.a.
≥16	n=147 (4.9%)	n=286 (4.2%)	n.a.	n.a.
Missing	n=22 (0.7%)	n=413 (6.1%)	n.a.	n.a.
Mean days admitted to hospital				
≤2	n=910 (30.5%)	n=1,943 (28.6%)	n.a.	n.a.
3-7	n=1,243 (41.6%)	n=2,343 (34.5%)	n.a.	n.a.
8-14	n=473 (15.8%)	n=1,375 (20.3%)	n.a.	n.a.
≥15	n=152 (5.1%)	n=615 (9.1%)	n.a.	n.a.
Missing	n=209 (7.0%)	n=511 (7.5%)	n.a.	n.a.
ICU-admission				
Yes	n=216 (7.2%)	n=434 (6.4%)	n.a.	n.a.
No	n=2,771 (92.8%)	n=6,353 (93.6%)	n.a.	n.a.
Missing	n=0 (0%)	n=0 (0%)	n.a.	n.a.

*Educational level was not collected in the group of non–responders of the injury cohort
$Educational level is based on the highest degree of education an individual has completed
Abbreviations: ICU=Intensive Care Unit, ISS=Injury Severity Score, ISS=Injury Severity Score, SD=standard deviation, yrs=years.

Comparisons between (pre-injury) HS of the injury and reference cohort

In both cohorts, males reported better HS compared to females. In general, people with low educational level revealed the lowest HS while people with high educational level revealed the highest HS.

In both the injury and reference cohort, the EQ-5D-3L summary score and EQ-VAS decreased when age increased. However, this trend was less apparent for the EQ-VAS of the reference cohort, especially in male participants. In almost all strata, injured patients reported better recalled pre-injury HS compared to the HS of the reference cohort (see **Table 2** and **Figure 2**). Female patients with low educational level aged 75 or older compromise a large proportion (12%) of the injury cohort. These patients showed lower pre-injury HS as compared with the HS of the reference cohort.

Table 2: Descriptive statistics of the (pre-injury) EQ-5D-3L utility score as completed by the injury cohort and as completed by the reference cohort. Results were stratified by gender, age and educational level

		Males				Females			
		Injury cohort		Reference cohort		Injury cohort		Reference cohort	
Age groups (yrs.)	Educational level	n	Mean (SD)	n	Mean (SD)	n	Mean (SD)	n	Mean (SD)
18-34	**Low**	44 (1%)	0.99 (0.05)	32 (2%)	0.93 (0.16)	24 (1%)	0.86 (0.22)	33 (2%)	0.85 (0.22)
	Middle	99 (3%)	0.96 (0.10)	91 (5%)	0.92 (0.15)	46 (1%)	0.94 (0.15)	139 (8%)	0.88 (0.17)
	High	44 (1%)	0.96 (0.12)	63 (3%)	0.97 (0.08)	35 (1%)	0.94 (0.13)	113 (6%)	0.89 (0.17)
35-44	**Low**	37 (1%)	0.98 (0.07)	15 (1%)	0.92 (0.11)	9 (0%)	0.94 (0.11)	18 (1%)	0.74 (0.37)
	Middle	63 (2%)	0.96 (0.08)	48 (3%)	0.93 (0.11)	33 (1%)	0.94 (0.12)	62 (3%)	0.88 (0.24)
	High	27 (1%)	0.99 (0.05)	50 (3%)	0.95 (0.12)	40 (1%)	0.95 (0.08)	60 (3%)	0.90 (0.20)
45-54	**Low**	88 (3%)	0.90 (0.20)	24 (1%)	0.90 (0.12)	67 (2%)	0.84 (0.27)	34 (2%)	0.74 (0.35)
	Middle	91 (3%)	0.96 (0.13)	42 (2%)	0.93 (0.11)	63 (2%)	0.89 (0.19)	54 (3%)	0.91 (0.14)
	High	75 (2%)	0.98 (0.06)	29 (2%)	0.95 (0.09)	44 (1%)	0.97 (0.07)	28 (2%)	0.91 (0.11)
55-64	**Low**	140 (5%)	0.88 (0.20)	31 (2%)	0.81 (0.25)	85 (3%)	0.89 (0.14)	42 (2%)	0.83 (0.22)
	Middle	119 (4%)	0.93 (0.13)	46 (3%)	0.89 (0.19)	62 (2%)	0.93 (0.10)	39 (2%)	0.89 (0.12)
	High	92 (3%)	0.94 (0.13)	40 (2%)	0.94 (0.16)	49 (2%)	0.97 (0.07)	47 (3%)	0.88 (0.17)
65-74	**Low**	145 (5%)	0.91 (0.15)	77 (4%)	0.90 (0.15)	190 (6%)	0.86 (0.20)	114 (6%)	0.85 (0.19)
	Middle	94 (3%)	0.92 (0.14)	60 (3%)	0.89 (0.18)	50 (2%)	0.83 (0.23)	42 (2%)	0.89 (0.14)
	High	93 (3%)	0.92 (0.14)	92 (5%)	0.93 (0.11)	46 (2%)	0.91 (0.14)	54 (3%)	0.88 (0.14)
≥75	**Low**	141 (5%)	0.81 (0.26)	28 (2%)	0.87 (0.13)	364 (12%)	0.74 (0.26)	46 (3%)	0.80 (0.21)
	Middle	62 (2%)	0.86 (0.15)	30 (2%)	0.84 (0.21)	64 (2%)	0.81 (0.21)	24 (1%)	0.81 (0.19)
	High	62 (2%)	0.94 (0.08)	38 (2%)	0.89 (0.15)	24 (1%)	0.89 (0.10)	9 (0%)	0.78 (0.22)

Abbreviations: SD=standard deviation, yrs=years.

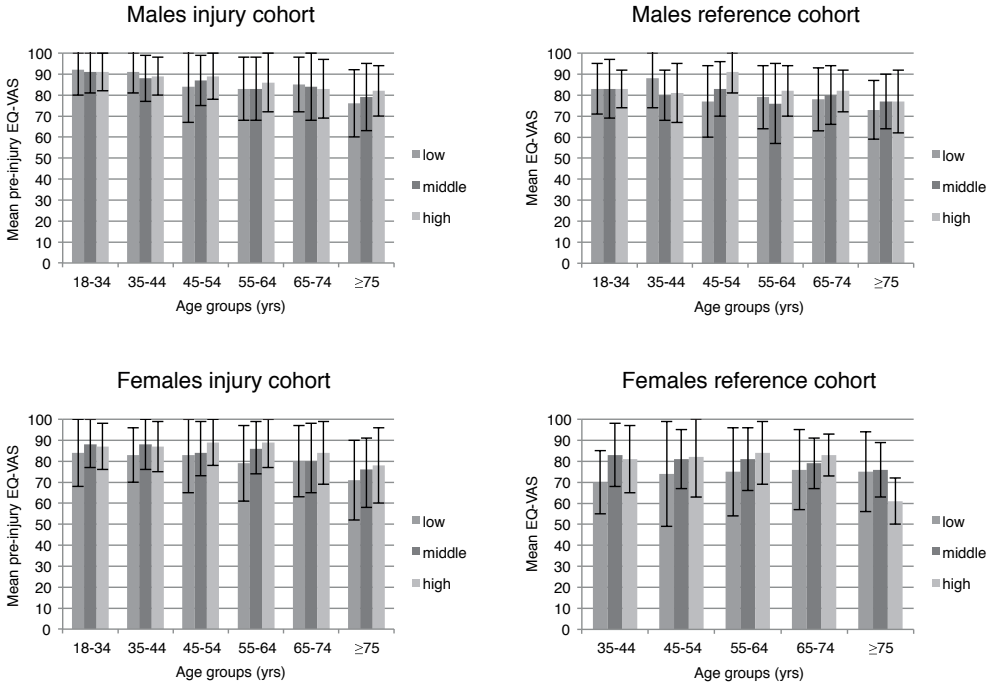

Figure 2: Mean (SD) (pre–injury) EQ–VAS of the injury and reference cohort classified by age, gender and educational level
Low educational level; reference cohort n=494, injury cohort n=1,389. Middle educational level; reference cohort n=677, injury cohort n=870. High educational level; reference cohort n=623, injury cohort n=642
Abbreviations: EQ–VAS= EuroQol Visual Analogue Scale, yrs.=years.

In the univariate analyses, all independent variables of interest were significantly associated with both the EQ-5D-3L summary score (p-value age <0.001, p-value gender <0.001, p-value educational level <0.001 (for middle educational level) and <0.001 (for high educational level)) and the EQ-VAS ((p-value age <0.001, p-value gender <0.001, p-value educational level <0.001 (for middle educational level) and <0.001 (for high educational level)). Therefore, all variables were entered into the multiple regression model.

Because gender might influence the association between educational level and HS (28), interaction terms between gender and educational level were included in the model to test for effect modification. For this, dummy variables were created for educational level (low educational level as reference group). Interaction terms between gender and educational level were statistically significant for both the EQ-5D-3L summary score (p-value=0.010 (for middle educational level) and p-value=0.028 (for high educational level)) and the EQ-VAS (p-value=0.008 (for middle educational level) and p-value=0.004 (for high educational level)). Therefore, results of the regression analyses were reported separately for males and females.

Multiple regression models were conducted with adjustment for age and educational level. The EQ-5D-3L summary score of the injury cohort was significantly higher compared to the summary

score of the reference cohort (β=0.020 [95% CI: 0.007, 0.033] for males and β=0.025 [95% CI: 0.007, 0.043] for females) (**Table 3**). The beta in block 3 increased ≥10% compared to the beta in block 2. The EQ-VAS was significantly higher in the injury cohort compared to the reference cohort (**Table 3**). When also adjusted for educational level, the beta increases <10% in males (from β=4.778 [95% CI: 3.617, 5.940] in block 2 to β=5.051 [95% CI: 3.881, 6.221] in block 3). However in females, the beta increases ≥10% (from β=3.635 [95% CI: 2.147, 5.123] in block 2 to β=4.189 [95% CI: 2.705, 5.672] in block 3). The ≥10% increment after the addition of educational level in the multiple regression analysis suggests that educational level is a confounder for HS, next to age and after stratification on gender.

Table 3: Multiple linear regression analysis of the (pre-injury) EQ-5D-3L and EQ-VAS

		EQ-5D-3L summary score	EQ-VAS
Block 1 Unadjusted	**Males**	β: 0.006 95% CI: -0.007, 0.019	β: 3.932 95% CI: 2.749, 5.115
	Females	β: -0.018 95% CI: -0.035, -0.001	β: 0.744 95% CI: -0.559, 2.248
Block 2 Adjusted for age	**Males**	β: 0.014 95% CI: 0.001, 0.027	β: 4.778 95% CI: 3.617, 5.940
	Females	β: 0.018 95% CI: -0.001, 0.036	β: 3.635 95% CI: 2.147, 5.123
Block 3 Adjusted for age and educational level	**Males**	β: 0.020 95% CI: 0.007, 0.033	β: 5.051 95% CI: 3.881, 6.221
	Females	β: 0.025 95% CI: 0.007, 0.043	β: 4.189 95% CI: 2.705, 5.672

Reference cohort=reference group.
Abbreviations: EQ–5D–3L= EuroQol–5D–3L, EQ–VAS= EuroQol Visual Analogue Scale, =unstandardized beta, 95% CI=95% Confidence interval.

For the logistic regression, significant differences in ORs were found for the 'self-care', 'pain/discomfort' and 'anxiety/depression' dimensions between the injury cohort and reference cohort (OR=1.655 [95% CI: 1.233, 2.221] for 'self-care', OR=0.564 [95% CI: 0.491, 0.647] for 'pain/discomfort' and OR=0.805 [95% CI: 0.671, 0.965] for 'anxiety/depression') after adjustment for age and gender (**Table 4**). The ORs of the 'mobility' and the 'daily activities' dimensions did not differ between both cohorts after adjustment for age and gender. When also adjusted for educational level, the injury cohort reported significantly more problems on the 'self-care' dimension (OR=1.497 [95% CI: 1.112, 2.016]) compared to the reference cohort. Furthermore, the injury cohort reported significantly less problems on the dimensions 'pain/discomfort' and 'anxiety/depression' (OR=0.522 [95% CI: 0.454, 0.602] for 'pain/discomfort' and OR=0.745 [95% CI: 0.619, 0.897] for 'anxiety/depression'). Compared to the beta in block 2 (adjustments for age and gender), the beta in block 3 (adjustment for age, gender and educational level) decreased in all dimensions. In line with the findings in **Table 3,** the beta in block 3 changed ≥10% compared to the beta in block 2 for all individual items of the EQ-5D-3L. This indicates that educational level is a confounder in addition to age and gender for all dimensions of the EQ-5D-3L.

Table 4: Logistic regression analysis of the individual dimensions of the (pre-injury) EQ-5D-3L

	Dimension 'Mobility' *No problems (=0) vs moderate/severe problems (=1)*	**Dimension 'Self-care'** *No problems (=0) vs moderate/severe problems (=1)*	**Dimension 'Daily activities'** *No problems (=0) vs moderate/severe problems (=1)*	**Dimension 'Pain/ discomfort'** *No problems (=0) vs moderate/severe problems (=1)*	**Dimension 'Anxiety/ depression'** *No problems (=0) vs moderate/severe problems (=1)*
Block 1 Unadjusted	β: 0.527 OR: 1.694 95% CI: 1.460, 1.966	β: 1.043 OR: 2.837 95% CI: 2.146, 3.749	β: 0.275 OR: 1.317 95% CI: 1.124, 1.543	β: -0.313 OR: 0.731 95% CI: 0.644, 0.830	β: -0.263 OR: 0.769 95% CI: 0.647, 0.914
Block 2 Adjusted for age and gender	β: 0.019 OR: 1.019 95% CI: 0.863, 1.203	β: 0.504 OR: 1.655 95% CI: 1.233, 2.221	β: -0.047 OR: 0.954 95% CI: 0.805, 1.132	β: -0.573 OR: 0.564 95% CI: 0.491, 0.647	β: -0.217 OR: 0.805 95% CI: 0.671, 0.965
Block 3 Adjusted for age, gender and educational level	β: -0.073 OR: 0.929 95% CI: 0.785, 1.101	β: 0.403 OR: 1.497 95% CI: 1.112, 2.016	β: -0.133 OR: 0.875 95% CI: 0.736, 1.041	β: -0.649 OR: 0.522 95% CI: 0.454, 0.602	β: -0.294 OR: 0.745 95% CI: 0.619, 0.897

Reference cohort=reference group
Male=reference group
Low educational level=reference group
Age=continue variable
Abbreviations: =beta, OR=Odds Ratio, 95% CI=95% Confidence interval.

DISCUSSION

This study reveals that retrospectively assessed pre-injury HS of the injury cohort is higher compared to the HS of the reference cohort. After adjustment for age, gender and educational level, there is still a bias in the measured pre-injury HS.

Our findings are in line with the results of previous studies in which a better HS was found in trauma patients as compared to a normative sample (15) or as compared to the general population norm (16, 17, 29, 30). We expect that the difference in HS between the reference cohort and the injury cohort could partly be explained by differences in educational level of the two cohorts. However, after adjustment for educational level (**Table 3**) and consequently by making the groups more comparable, the difference in reported HS between the injury and reference cohort further increased. The contribution of differences in educational level might partially cancels out the (positive) effect of other unmeasured confounders. Also as in our study, previous findings revealed better pre-injury outcomes predominantly in younger patients (29). A higher activity level increases the risk of an injury (31). Additionally, a higher activity level may also contribute to a better HS, leading to a healthy worker effect in the injury cohort. Subsequently, HS of the general population might underestimate the pre-injury HS because of a higher level of activity on the part of the trauma population. Besides, as stated in the introduction, retrospectively collected data can be distorted due to recall bias (7). Due to the large impact an injury might have, patients generally overestimate their HS prior to their trauma (6). Previous research also found that demographic characteristics such as age or educational level influence recall accuracy (32).

There is a lack of a clear definition of SES and there are large differences in methodology to determine SES. Today, educational level is used most frequently to indicate SES (33).

The trauma population is an ageing population. In this study, 12% of the responders of the injury cohort included elderly females with low educational level. Subsequently, the HS as reported by this group of patients might have influenced the study findings.

In contrast to previous studies amongst representative German and English study samples (34, 35), the reference cohort in our study showed no clear trend on the EQ-VAS when participants were categorized by low, middle or high educational level.In contast to the five dimensions of the EQ-5D-3L which ask about very specific functional states or activities, the VAS is a very subjective assessment of HS.

The impact of a trauma can largely influence patients' internal standards (36). Compared to the reference cohort, the injury cohort reported significantly less problems on the 'pain/discomfort' and 'anxiety/depression' dimensions, but reported significantly more problems on the 'self-care' dimension. The health states of the EQ-5D-3L are converted into a summary score by applying a formula that adds values (i.e. weights) to each of the levels in each of the five dimensions (24). Therefore, the EQ-5D-3L does not reflect all dimensions of HS equally and subsequently, it is important to examine the multiple components of HS.

Limitations

For the Netherlands, general EQ-5D population norm scores by age and gender category are available (37). Comparison of the HS of the reference cohort and the Dutch general population norms showed that the general norm scores deviated from the HS of the reference cohort (data not shown). In the majority of the strata, better HS was found in the reference cohort. This raises the question regarding the representativeness of the reference cohort in our study. However, since we used strata for the comparisons and since we corrected for age, gender and educational level in the regression analysis, we argue that this does not have a large influence on the study results. Secondly, the response rate of the injury cohort was low (31% of the total eligible injured population). Patients with a very minor injury (ISS 1-3), patients with a mild injury (ISS 9-15) and those who were admitted ≥8 days were less likely to participate into our study. The responders and non-responders of the injury cohort differed largely according to age and gender. Thirdly, we had no information of the non-responders of the injury cohort regarding educational level, which apparently can lead to selection bias. Consequently, the respondents' pre-injury HS is most probably not representative of the pre-injury HS of the population we intended to analyse. Fourth, due to the different timing assessments of HS prior to the trauma, results might be biased (12). Fifth, we cannot exclude change findings due to multiple testing. Change findings might particular have occured for the results of the individual domain scores of the EQ-5D-3L.

Recommendations for future research

This study leads to new research questions. More research is needed to examine whether a more earlier assessment might minimize the high pre-injury HS. Researchers should also find explanations for the increased differences between pre-injury HS and HS of the reference cohort after adjustment for educational level. Apart from age, gender and educational level, factors such as occupational status (38), living alone or not (38), activity level (31) or the presence of comorbidities (39-41) can influence HS as well. In all probability, these known (and other still unknown) characteristics differ amongst the injury and reference cohort. More research is necessary to examine which differences in characteristics exist between injury and reference cohorts and future research is vital to examine the influence of these characteristics on HS.

CONCLUSIONS

Without adjustments as well after adjustment for both age, gender and educational level, injured patients report better recalled pre-injury HS compared to the HS of a reference cohort. After adjustment for educational level, the difference in HS between the injured population and the reference cohort increases. This underlines that other confounders might also influence HS.

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6

Chapter

Perceived changes of Quality of Life in trauma patients: a focus group study

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Journal of Trauma Nursing 2018;**25:**3
DOI: 10.1097/JTN.0000000000000364

ABSTRACT

Quality of life (QoL) following a physical trauma is still insufficiently known from a patient perspective. The aim of this study was to qualitatively report perceived changes in QoL after trauma. Focus groups were conducted. Patients admitted to the hospital were eligible for inclusion if they had a lower extremity trauma, severe injuries or severe traumatic brain injury (TBI). Patients 75 years or older were invited. To analyze the perceived changes in QoL, open coding was used. Patients (n=20, mean 55y) reported comparable consequences. In the first month post-trauma, physical limitations, independency, pain and anxiety predominated. Later, patients experienced problems with acceptance. The patients' feelings of the need to have control over their own situation, their own expectations and a social network were related to QoL. Compared with the other patient groups, TBI patients reported more psychosocial consequences and elderly patients reported more difficulties in performing (social) activities. Quality of health care was considered an important aspect in the patients' perceived QoL and adequate aftercare was missed according to the patients. The impact of a trauma influences QoL in different health domains. Further improving the quality of aftercare may positively influence trauma patients' perceived QoL. These results indicated that TBI patients and elderly patients deserve specific attention regarding QoL.

Keywords: focus groups, non-fatal outcome, QoL, qualitative methods, trauma

INTRODUCTION

According to the World Health Organization (WHO), trauma is a major and worldwide problem and continues to place a tremendous burden on public health (1). The trauma mechanism and trauma type can be diverse, and there is a large variety of factors including regarding age, gender, and socio-economic status, that indicate the heterogeneity of the population. Recently, the in-hospital mortality rate of trauma patients in the Netherlands was 2% (2). Consistent with this finding, a large proportion of patients survive their trauma and have to address the remaining physiological and physical changes, which can have a large effect on the patients' life. For example, physical limitations can lead to difficulties in performing daily activities or to problems in partnership or other social relationships.

Quality of Life (QoL) is a subjective phenomenon; it aims to measure the patients' satisfaction with their functioning. QoL is a multidimensional concept, including both positive and negative aspects of life. It incorporates a person's physical health, psychological state, level of independence, social relationships, personal beliefs and relationship to salient features of the environment (3).

However, little is known about the factors that play a role in the patients' perceived QoL after trauma. Uncertainty about recovery was considered stressful for trauma patients who reported longer-term pain, resulting in a large decrease in QoL (4). Furthermore, injury, specifically in the elderly, can lead to an ongoing process of isolation and activity restrictions via insecurity, misgivings and fear, which negatively influence their QoL (5).

Conducting focus groups is necessary to understand trauma patients' QoL since focus groups can provide a deeper understanding of complex insights. Therefore, the aim of this study was to gain more insight into changes in perceived QoL after trauma via a direct exploration of the patients' point-of-views.

METHODS

This study was approved by the Ethics Committee Brabant (the Netherlands), project number NL50258.028.14. The study was performed in accordance with the 1964 Helsinki declaration.

Participants

Adult patients were selected by one author (NK) from the Brabant Trauma Registry (BTR) database. Patients were selected based on severity and type of injury using the Abbreviated Injury Scale (AIS) and Injury Severity Score (ISS). The AIS is used to define the anatomical region and severity of separate injuries in detail (range from 1–6). The ISS is used to assess the overall trauma severity ranging from 1–75. An ISS≥16 is considered severely injured (6).

Patients were eligible to participate if they were admitted in 2014 to a ward or the intensive care unit (ICU) of the Elisabeth-TweeSteden Hospital (Tilburg, the Netherlands), a Level 1 trauma centre. The group of included patients had to be a representative sample of the trauma population. To meet this criterion, patients who were invited to attend a focus group were randomly selected based on gender, age and type and severity of the trauma. The trauma population is a heterogeneous population. Therefore, four different subgroups of patients were

created that represented, in our opinion, a good reflection of the total population. We recruited (a) patients ages 18–64 years with a blunt trauma of the lower extremity, with an ISS<13 and without other serious injuries; (b) patients ages 75 years or older with an ISS<16; (c) patients ages 18–64 years with a blunt trauma, with an ISS≥16 (i.e. severely injured); and (d) severe traumatic brain injury (TBI) patients ages 18–64 years with an AIS-head≥4 and admitted to an ICU. Exclusion criteria were (1) pre-existing severe cognitive deficits and (2) an insufficient knowledge of the Dutch language. Purposive sampling was used, meaning that the recruitment of patients was completed after the intended number of patients and sufficient diversity between the patients in the focus groups was achieved. Due to the small number of patients selected from the BTR who were willing to participate, additional patients were selected by a trauma surgeon (K.W.W. Lansink, MD, PhD) via screening of medical health records.

Procedure

In the focus group, the participants discussed and debated their experiences about a specific topic. Additional focus groups were conducted if the most recent group provided new information until a focus group no longer provided new information (saturation point is reached) (7). Before participation, all patients signed an informed consent form. The focus groups were conducted by two researchers (NK and MT).

Audio-records were made during each focus group. A script was developed and the average scheduled duration of each focus group was two hours. During the focus groups, three questions were included:

- *'What is QoL in your opinion?'*
- *'Which short- and/or long-term consequences did/do you experience after your trauma?'*
- *'Which aspects or facets determine your QoL after your trauma?'*

If a different subgroup of patients (e.g. TBI patients, severely injured patients or elderly patients) reported consequences that were related to their specific type of injury or age, then these consequences were reported separately in the results section.

Data analysis

To analyze perceived changes in QoL, open coding was used. All audio-recorded data were transcribed verbatim. Two authors (NK and MK) independently read and coded each of the transcripts using Microsoft Word and Excel. First, the researchers determined the beginning and the end of each fragment using track changes. Second, the researchers independently determined why each fragment was considered a meaningful whole (i.e. text which belongs together and addresses one issue or idea). Third, the researchers independently judged whether the fragment was relevant to the research topic. If this was the case, then the codes were assigned to the text fragment. Fourth, using Excel, the different fragments were compared to examine whether the multiple fragments in the text addressed the same topic and should therefore receive the same code (8, 9). Any discrepancies in coding were resolved via discussion until a consensus was reached or by consulting a third author (MT). In the text, the major and important findings of the focus groups are outlined.

RESULTS

In total, 98 patients were invited to participate in the focus groups (see **Figure 1**). TBI patients showed large willingness to participate. Therefore, two focus groups were created with this group of patients (round 1: n=5 and round 2: n=7). Due to the small number of interested patients in the remaining groups it was necessary to combine the groups. Two focus groups with severely injured patients and elderly patients were combined (round 1: n=4 (n=3 severely injured, n=1 elderly) and round 2: n=4 (n=2 severely injured, n=2 elderly)). Twenty patients participated in the four focus groups.

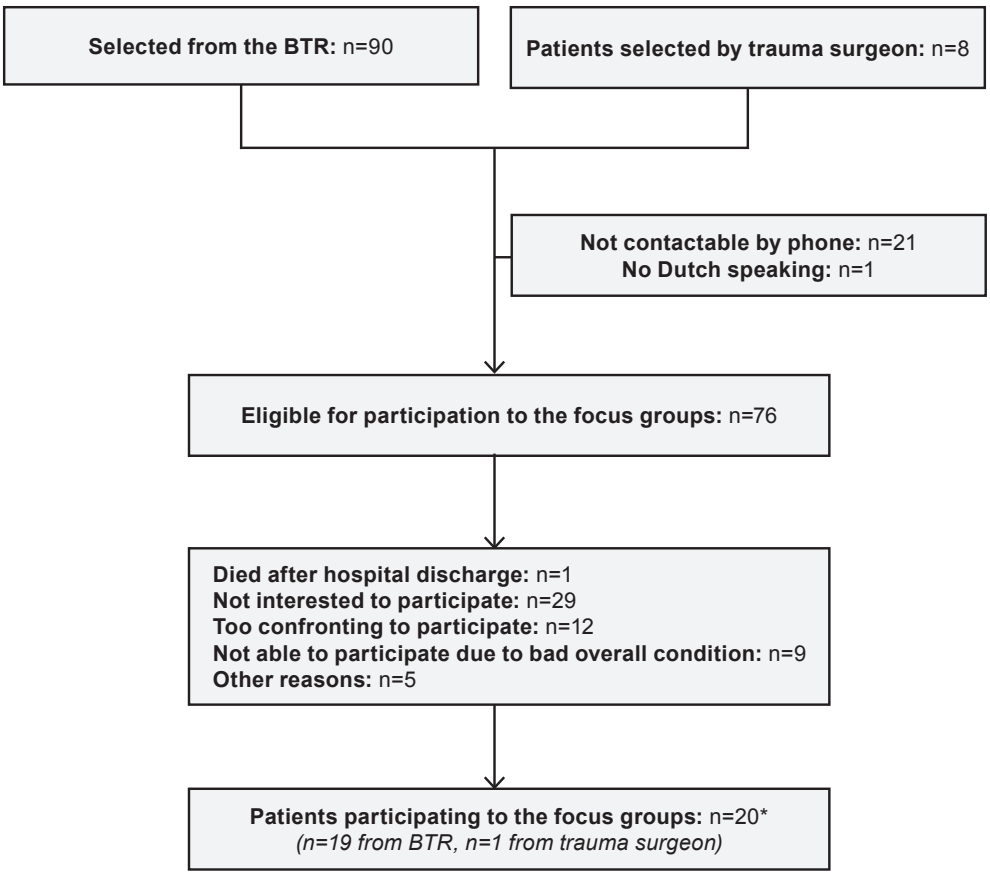

Figure 1: Flow diagram of trauma patients invited to participate in the focus groups
*Of these participants, 4 were accompanied by their informal health care giver since patients' poor physical or psychological functioning
Abbreviations: BTR, Brabant Trauma Registry.

Table 1 provides an overview of the demographic characteristics of the participants. Three TBI patients and one elderly patient were unable to attend the focus groups without the assistance of an informal caregiver due to their poor functioning. Therefore, partners of these patients were allowed to accompany the patients. Partners were not actively involved during the focus groups, although at the end of each focus group, the partners were given the opportunity to submit remarks.

Table 1: Demographic characteristics of the focus group participants

Characteristics	Mean, ±SD
Age* (yrs.)	55 (±16, range 28-81)
ISS98	23 (±10, range 6-45)
Length of hospital stay (d)	18 (±19, range 2-86)
Time since injury (mo)	17 (±2.46, range 13-21)
	n (%)
Gender	
Male	12 (60%)
Female	8 (40%)
Educational level	
University degree	4 (20%)
Bachelor's degree	5 (25%)
Senior secondary vocational education and training	6 (30%)
Preparatory secondary vocational education	5 (25%)
Household	
Single household	6 (30%)
Multiperson household	14 (70%)
Injury cause	
Road traffic injury	11 (55%)
Fall	7 (35%)
Work-related	1 (5%)
Sport-related	1 (5%)
Injury mechanism	
Blunt	20 (100%)
Penetrating	0 (0%)
ICU admission	
Yes	16 (80%)
No	4 (20%)
Currently working	
Yes	10 (50%)
No	10 (50%)

*time of the trauma

Abbreviations: d, days; ICU, Intensive Care Unit; ISS98, Injury Severity Score 98; mo, months; yrs, years.

Definition of QoL according to trauma patients

First, patients were asked to provide a definition of the term 'QoL' (see **Table 2**). Participants emphasized that QoL is a subjective phenomenon and incorporates different aspects; for the participants, QoL mainly incorporated not being dependent on someone, enjoying life and being able to perform activities of daily living.

Table 2: Trauma patients' thoughts about the term 'QoL'

Quotes
• *"The way you live your life and how you deal with it. … Whether you need help of someone else and whether you can live more or less independently."* (F, 81y, fall, elderly patient)
• *"Being together with other people, enjoying life, having fun, getting help from others when necessary and being satisfied. I find it really important that I can do whatever I need to do, or want to do, without suffering any pain."* (F, 61y, sport-related accident, severe injury)
• *"Being independent… enjoying the things you are still able to do."* (F, 64y, road traffic accident, severe TBI)
• *"I think mainly about the normal things of life, whether they are still possible … Can you cook, can you do the laundry, can you take your children to school, in fact the very normal daily things, can you manage those, yes or no? … For me, QoL means being independent."* (M, 43y, road traffic accident, severe TBI)

Abbreviations: F, female; M, male; TBI, traumatic brain injury; QoL, Quality of Life; y, year.

Consequences and perceived changes in QoL after trauma

During the discussions, the two leading questions *'Which aspects of facets determine your QoL after your trauma?'* and *'Which short- and/or long-term consequences did/do you experience after your trauma?'* often overlapped in the answers the participants provided. Therefore, these results were combined (see **Table 3**).

Overall QoL and health

These results showed that most patients irrespective of trauma severity, trauma mechanism, or age reported the same consistent consequences, including many physical, psychological, social and environmental issues. Nearly all of the patients stated that their QoL had been changed after the trauma. During the focus groups, five patients stated that they were still rehabilitating. In the first months post-trauma, nearly all patients reported that their own feelings (i.e. their emotional perception or attitude such as anger or sadness) and their own expectations largely influenced their recovery. Eight participants clearly indicated that their feeling of having control over the situation positively influenced their recovery and other patients agreed with this statement. In the long-term, patients experienced difficulties with accepting their remaining disabilities and their new life. Patients acknowledged that they have to live with the long-term physical and psychological consequences of their injury. Three patients stated that they did not allow their injury to play a dominating part in their remaining lives. However, most patients concluded that their trauma has changed their life since the consequences of their injury had a negative impact.

In comparison to other patient groups, TBI patients reported more psychosocial consequences such as personality changes. Two elderly patients stated that QoL was highly related to their age. For these patients, increasing health problems, loss of function and a high risk of being dependent on someone else were seen as normal parts of their ageing process. Compared to the other patients, all three elderly patients reported less functional impairments but reported more problems in performing (social) activities.

Table 3: Trauma patients' perspective on perceived changes in QoL

General QoL and health
• *"I've to look at the here and now and which steps I want to be able to take for tomorrow and well the old stuff, it will never be the same again anyway. So, let all that go and enjoy the little normal things in life. But it's much easier said than done."* (M, 43y, traffic accident, severe TBI)
• *"I have now reached a point where I have to act or think about the activities that I can perform rather than the things I cannot do. And I think that you've come a long way when you can do that."* (M, 80y, fall, elderly trauma patient)
• *"I've put my life as it was before my trauma behind me and I went on with other things. I had to do it for my own good."* (M, 46y, fall, severe injury)
• *"I felt down and self-absorbed but at a certain moment I changed my mind. I thought Damn it! Come on, look at it from a different perspective! From that moment, I made huge steps forward... I am absolutely certain that psychological functioning influences physical functioning."* (M, 46y, fall, severe injury)
• *"Recovery is more, I rather think it is more about your psychological functioning than about the physical area, the one cannot function without the other.."* (F, 42y, road traffic injury, severe injury)
• *"It's nice that people take good care of you physically during your hospital stay. They helped me very well. But actually, many things come after that part. And that doesn't all have to be negative… . Acceptance, that did not happen until one year after my trauma… after the second opinion when I heard that nothing could be done about it… . It's hard to know that you are powerless to do anything about it."* (F, 42y, road traffic accident, severe injury)
Physical health
• *"I live with constant pain, ad nauseam." (M, 37y, road traffic accident, severe TBI)*
• *"My 'battery' is always empty…." (M, 43y, traffic accident, severe TBI)*
• *"I was always in a hurry and doing things quickly and now I take a little more time." (F, 81y, fall, elderly patient)*
• *"I'm tired, I'm extremely tired. I'm tired and I can't sleep." (M, 37y, road traffic accident, TBI)*
• *"I notice that I can go to bed very tired and still lie awake for three or four hours." (F, 64y, road traffic accident, severe TBI)*
• *"I had to use a wheelchair and I was devastated about that." (M, 79y, fall, elderly trauma patient)*
• *"After my accident I became dependent on other people… . Independency is clearly important to me." (M, 43y, work-related accident, severe injury)*
• *"Before my accident I did everything by myself. Now I need help with almost everything." (M, 56y, road traffic accident, severe injury)*
• *"I thought that I received very good medical care during the entire process and I actually still think so today." (M, 56y, road traffic accident, severe injury)*
• *"In my opinion the care I received was really very good and particularly the facilities in the hospital, which have improved so much that I really didn't mind being in hospital." (M, 79y, fall, elderly trauma patient)*
• *"Many activities were rather exhausting because I received many external stimuli and I really couldn't handle them yet." (M, 28y, road traffic accident, severe TBI)*

Table 3 *(continued)*

Psychological health
• *"My life now is much better than my life before my trauma. Always being busy and having to do 100.000 things at the same time and now I just can't do it anymore."* (F, 64y, road traffic accident, severe TBI)
• *"I'm currently working hard to achieve everything that's possible for me, I refuse to become a victim because of my trauma."* (F, 58y, fall, severe TBI)
• *"I've learned how nice it can be to just look outside and watch the birds."* (F, 61y, sport-related injury, severe injury)
• *"About 'what happened yesterday'? Before my accident I would just know that immediately. Now I've to really search my memory, what happened yesterday. That's new for me."* (F, 61y, road traffic accident, severe TBI)
• *'What did I do to my partner and children? I was the one who climbed onto that motorcycle."* (M, 43y, road traffic accident, severe TBI)
• *"Balance and recovery of the body and automatic compensation of the body. I think it is rather surprising that my body …just nice to see how my body has recovered."* (F, 42y, road traffic accident, severe injury)
• *"I've got another scar and that seems to be attractive."* (M, 56y, road traffic accident, severe injury)
• *"The realization that my accident happened and that it can happen again."* (F, 61y, sport-related injury, severe injury)
• *"The only thing for me is that I have become extremely cautious at work. Nothing has a ctually changed, but what happened is constantly at the back of my mind."* (M, 43y, work-related accident, severe injury)
• *"Fear of pain. Purely based on ignorance, really."* (F, 42y, road traffic accident, severe injury)
• *"The things I did before in one day, I would not mind doing them in three days now. But the fact that I just can't do them anymore, that's really painful."* (M, 56y, road traffic accident, severe injury)
• *"I've really become more emotional but I don't see that as a shortcoming or a flaw. Nowadays I'm more guided by my intuition."* (M, 43y, road traffic accident, severe TBI)
Social relationships
• *"My trauma led to unexpected consequences; changes in my relationship with my partner and my children. And there is a new kind of fear: will it be all right again?"* (M, 43y, road traffic accident, severe TBI)
• *"Since my accident I like to be on my own."* (M, 37y, road traffic accident, TBI)
• *"They say: 'Oh, I recognize your situation, I really do' but they are healthy!"* (F, 64y, road traffic accident, severe TBI)
• *"Well if you break a leg and they take a radiograph then you need to get a plaster cast. I think that they think they understand my situation but they don't."* (F, 58y, fall, severe TBI)
• *"People sometimes don't understand my situation. They say: 'Oh, you look great! You can do everything now'."* (F, 81y, fall, elderly patient)
• *"A lot of people payed attention to my situation, I had never experienced that before. Everybody wanted to know how I was doing. People asked: 'Can we do anything to help?'. That was really overwhelming! … Then I started thinking; this is really great, to have people around me who are concerned about me, who did not just ask how I was doing and then disappear into thin air but who kept calling me all the time, that was really wonderful!"* (M, 79y, fall, elderly trauma patient)

Table 3 *(continued)*

Environment
• *"I'm more aware of the dangers, I've become more cautious."* (F, 42y, road traffic accident, severe injury)
• *"After my accident, our house was remodeled, so we can now sleep downstairs… I can do everything downstairs, so I don't have to go upstairs anymore, which would be difficult anyhow."* (F, 81y, fall, elderly trauma patient)
• *"After my accident I needed a modified car and I needed to start all over again learning how to drive a car. It cost me a lot of money that I didn't take into account beforehand. … After all, the counterparty compensated all these costs. But imagine that you've to pay the costs all by yourself!"* (M, 56y, road traffic accident, severe injury)
• *"I would have preferred the orthopaedic surgeon to say: 'Let's plan another appointment half a year from now, so we can make a new X-ray and check how you are doing and what possible consequences there might be, positive or negative'. And that did not happen! The treatment just ended. That's really important to me."* (M, 79y, fall, elderly trauma patient)
• *"A few months after my accident I had a standard bone scan and that was all fine. My shoulder also recovered very well, but my head just would not heal. … I suffer from my brain injury. I immediately got the results of the bone scan, but I said 'I would rather have had my head examined'."* F, 81y, fall, elderly trauma patient
• *"Bureaucracy slows everything down. Frustration about the municipality…. All those troubles with the public authorities, that it takes forever and that you are actually actively opposed by them."* (M, 46y, fall, severe injury)
• *"A trauma can teach you to become healthy again."* (M, 43y, road traffic accident, severe TBI)
• *"For a long time I was dependent on a taxi, or on a scoot mobile, or I had to ask my family or friends to drive me. Loss of mobility is really terrible."* (M, 56y, road traffic accident, severe injury)
• *"I wasn't eligible for a compensation for the costs for a taxi… I couldn't do anything; I was not allowed to drive a car or to ride a bike. However, I had to go to therapy. My neighbour aged 80 took me to therapy in his car."* (F, 64y, road traffic accident, severe TBI)

Abbreviations: F, female; M, male; TBI, traumatic brain injury; y, year.

Physical health

All groups thoroughly discussed the physical consequences. The overall consequences were comparable among all groups. An important cause of the physical limitation was pain. All participants stated the importance of being independent. Performing activities of daily living, such as getting dressed, was considered very important. Patients frequently reported a lower level of energy and reduced work capacity. All TBI patients reported memory impairments, fatigue, sleeping problems, difficulties with stimulus processing and speech difficulties (e.g. aphasia).

Psychological health

Patients reported several psychological consequences that mainly included negative feelings. Fear of receiving a new trauma was present for most participants. Some patients emphasized that their injury negatively influenced their emotional well-being; the trauma affected their lives dramatically since they were unable to return to their normal physical functioning as before their injury. Nearly all participants expressed that the psychological shock after trauma still remained even after more than 1 year post-trauma. Except for a few patients, the changed life situation led to problems with acceptance. Patients described disappointment over the remaining limitations. In contrast, in each of the focus groups at least one participant spoke about the positive aspects of their trauma (i.e. posttraumatic growth). Since the trauma, the patients can see and enjoy more easily the little things in life.

All TBI patients reported that they still experience many psychological problems of which irritability was considered to be the most important. Other reported psychological problems were sadness and difficulties with emotion regulation (e.g. crying more easily for no reason).

Social relationships

Except for one TBI patient, all patients stated how important family and friends were for their recovery. The possibility to obtain assistance from others was considered very important during recovery. Soon after their trauma, most patients received abundant of social support and the patients felt positively overwhelmed by this support. However, for one elderly patient, a loss of mobility resulted in activity restrictions and a more isolated life on the long-term post-trauma. The consequences of the trauma were not limited to the patients. TBI patients shared that their physical and psychological consequences affect not only themselves but their family members as well. Relatives stated to the patients that their personalities have been changed.

All TBI patients emphasized that it was difficult to explain their situation over and over again to others. They shared the view that their psychological symptoms were often not taken seriously by others who are unable to understand the problems that face TBI patients.

Environment

Different changes in the environmental domain (e.g. access to and quality of health-care and financial resources) were discussed. All participants stated that good communication skills and empathy of health-care providers positively influenced their recovery process and this contributed indirectly to the trauma patients' perceived QoL. However, nine patients clearly felt that they were not well informed about their situation. TBI patients emphasized that health care professionals should involve their close relatives more. Furthermore, all patients stated the importance of an appropriate follow-up. However, aftercare in the sense of outpatient monitoring was often not offered although the patients felt that they needed it. The lack of a follow-up indirectly influenced the patients' QoL negatively.

Eight patients felt that the laws and regulations were not fitted to their situation. Examples included difficulties during their process to return to work (RTW) or by requesting a parking license for disabled people. Patients' shared experiences focused predominantly on the cumbersome procedures and incomprehension of the public authorities. Insufficient financial resources also had a negative influence on the patients' QoL. In particular, in the elderly group, patients had to (partially) pay for medical aids such as a walking aid or braces in the bathroom. Two patients had difficulties into paying for these aids.

All patients who were employed before their injury reported difficulties with RTW. Large difficulties with RTW were specifically reported by TBI patients. Participants who worked before their injury stated that having a job is not only an aspect of physical or psychological health; these patients felt that RTW was associated with having a place in the society again.

Participants agreed that good transportation facilities made it easier to be active and social. Nine participants became long-term or permanently dependent on others to bring them to social activities, leading to a reduction in perceived QoL. This aspect was particularly important for elderly patients.

Partners' experiences of changes in QoL after trauma

Four patients were unable to attend a focus group without the assistance of their caregiver. Partners were shortly given the opportunity to report the consequences that they experienced (see **Table 4**). Partners reported consequences that overlapped with the patients' reported consequences. All partners would like to be more actively involved and would like to have more information about the patients' hospital stay and expected recovery process. Furthermore, all partners stated that the trauma influenced their lives as well since they had to accept their new lives as being a partner of a person with disabilities.

The partners of TBI patients named several psychosocial consequences that the patients did not mention in precise detail during the focus groups, for example, personality changes. The partners stated that the patient was not always aware of the consequences of the brain injury and subsequently, they had to confront the patient with these changes. Moreover, some of the psychological consequences of the TBI patients were perceived differently by partners. For example, one partner stated that his relative had severe difficulties following a storyline; however, the patient partially agreed with this.

Table 4: Perceived changes in QoL of trauma patients' partners

Quotes partners
• *"His trauma has serious consequences for us; we are not able to go on holiday anymore, he now can't take a shower without assistance and he can't walk anymore."* (Partner of M, 80y, fall, elderly trauma patient)
• *"(My husband) had his last surgery nine weeks ago. And I realize that I only started to come to terms with it after that operation. Before that, there just was no space for it… ."* (Partner of M, 43y, road traffic accident, severe TBI)

Abbreviations: F, female; M, male; TBI, traumatic brain injury; y, year.

DISCUSSION

This study shows that trauma influences patients' QoL in different health domains. Most of the physical, psychological, social and environmental consequences after a trauma are the same in all patients irrespective of age, trauma mechanism, or severity. Time after the injury plays an important role in the patients' way of experiencing QoL. In the first months post-trauma, patients stated that their feelings and expectations largely influenced their recovery and QoL and vice versa. Participants stated that their feeling of having control over the situation positively influenced their recovery, although some patients felt that they had no control on their recovery. Furthermore, physical limitations, independency, pain and anxiety dominate. In the long-term, patients experienced difficulties with accepting their remaining disabilities.

Trauma patients stated that QoL is largely dependent on independency and being able to perform daily activities. Throughout the recovery process, it became evident for patients that some consequences would remain for the rest of their lives. However, some patients stated that the trauma had positively changed them, by increasing the potential to see and enjoy more easily little things in life. Perceived changes in QoL in trauma patients showed similarities with changes in QoL in other patient groups. For instance, trauma patients reported difficulties in accepting their new life and this was also found in patients with Parkinson's Disease, stroke, or in patients after a kidney transplantation (10-12).

The emotional impact of the consequences of a trauma can differ per person. Consistent with the literature, the feeling of having control over the situation, the patients' own expectations and attitude (e.g. belief in own ability to address with problems) can have a large influence on perceived QoL (13-16). For example, a problem-solving person might encounter problems with adjusting to their limitations, as they may find it difficult to accept their situation. This study reveals that stage of life also plays an important role. Due to their high age, elderly patients stated that their needs and desires were reduced regarding functional outcome. For the working age population, RTW was clearly important which confirms conclusions from previous trauma research (17).

Furthermore, this study underlines the importance of a strong social network and sufficient societal support. A good social network is vital since patients often experience difficulties with daily activities such as self-care. Reductions in QoL can be expected when there is lack of social support. This finding is consistent with earlier studies demonstrating that social support tends to be of great importance to the well-being and recovery process of trauma patients (4, 8, 18-20). With regard to societal support and finances, the patients often feel that they stand alone. Patients become dependent on others due to the different laws and regulations from the public authorities and this outcome is consistent with an earlier study amongst spinal cord injury patients (21). As in the case of other patient groups (10, 22), some trauma patients experience difficulties in buying medical aids. To optimize the patients' QoL, public authorities (e.g. government authority) should improve standard processes by taking into account the patients' individual needs.

This study revealed that trauma can also have a negative impact on the partners' life, specifically in TBI patients. Partners of TBI patients have to alert their relative about the acquired shortcomings and this outcome is consistent with previous research (23, 24). Moreover, in earlier studies, caregivers reported changes in relationships with patients, which negatively influenced their QoL (23, 24).

Quality of health-care is an important aspect in the patients' perceived QoL. Participants emphasized the need of appropriate aftercare in the form of outpatient monitoring to identify their remaining problems. This finding is consistent with earlier research among different patient groups in which a good quality health-care system had a large influence on the patients' QoL (4, 10, 25).

The results of this study indicate that more awareness in health care settings is necessary to optimize trauma patients' QoL. In recent studies, the role of a case manager or nurse coordinator has proven to be effective in oncology patients but also in patients with acquired brain injury (26, 27). From hospital admission until discharge, a case manager can function as a first contact person for patients and before leaving the hospital, a conversation with the case manager is offered to the patients. This case manager can provide information about the trauma and expected recovery while taking into account the patients' expectations. In addition to care coordination, it is recommended to extend the standard aftercare to screen the remaining problems that the patients have to address, for instance trauma-related psychosocial or emotional issues (e.g. adjustment issues or a post-traumatic stress disorder (PTSD)). A large proportion of the patients suffer from psychological impairments, which can have a large negative effect on their recovery and QoL (28). For example, after three months, a follow-up appointment with a case manager can be offered to support and advise patients and their relatives to accept their new life situation. A less invasive alternative is that this extended aftercare can be offered by a general practitioner to signpost patients. If necessary, the patients can be referred to an appropriate (health) service.

Previous studies concluded that specialized trauma nurses have a significant impact on the care and management of trauma patients during their hospitalization (29). Trauma nurses can play an important role during the patients' hospitalization since the nurses can inform and advise patients and their relatives when they are uncertain or worried about their future.

This study has its limitations. It was necessary to combine the different subgroups of patients who were created beforehand because of the small number of patients who were willing to participate. Subsequently, this small number might have led to response bias. Another limitation is selection bias since only Dutch-speaking participants could participate. Reported QoL might be underestimated because several patients stated that their participation was too confrontational and others were unable to attend the focus group because of their bad overall condition. Despite these conditions, the included participants demonstrated a large range or characteristics in age, trauma mechanism and severity.

This study provides recommendations for future research. First, the patients' own expectations had a large influence on perceived QoL. Therefore, more research is necessary to examine the patients' information needs with regards to symptoms and recovery. Subsequently, information protocols can be developed. Second, research should focus on the psychological well-being of family members confronted with an injury of their relative, especially in TBI patients. Third, patients with the same clinical condition can report different QoL scores. Researchers should take into account trauma patients' feeling to have control over the situation and the patients' own expectations when examining QoL. Lastly, this study indicated the necessity for specific attention for two specific injury groups when examining patients' QoL, i.e. elderly patients and TBI patients. The main focus in elderly patients needs to be on measuring the changes on the (social) activity level. For TBI patients, the focus should be on psychosocial problems.

CONCLUSION

Time since injury plays an important role in the patients' way of experiencing QoL. This study shows that trauma influences QoL in different health domains. The trauma patients' social network and quality of health-care play an important role in the patients' QoL experience. Trauma nurses can play an important role in improving the trauma patients' perceived QoL by informing and advising patients.

ACKNOWLEDGEMENTS

We thank Bonnie Biesbroeck for her assistance with one of the focus groups. We thank Lieke Meuleman and Rubén Amatuni for the transcriptions of the focus groups.

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7

Chapter

Validation and reliability of the Abbreviated World Health Organization Quality of Life Instrument (WHOQOL-BREF) in the hospitalized trauma population

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Injury 2018;**49:**10
DOI: 10.1016/j.injury.2018.08.016

ABSTRACT

Introduction: While the number of trauma patients surviving their injury increase, it is important to measure Quality of Life (QoL). The Abbreviated World Health Organization Quality of Life (WHOQOL-BREF) questionnaire can be used to assess QoL. However, its psychometric properties in trauma patients are unknown and therefore, we aimed to investigate the validity and reliability of the WHOQOL-BREF for the hospitalized trauma population.

Methods: Data were derived from the Brabant Injury Outcome Surveillance. Floor and ceiling effects and missing values of the WHOQOL-BREF were examined. Confirmatory factor analysis (CFA) was performed to examine the underlying 4 dimensions (i.e. physical, psychological, social and environmental) of the questionnaire. Cronbach's alpha (CA) was calculated to determine internal consistency. In total, 42 hypotheses were formulated to determine construct validity and 6 hypotheses were created to determine discriminant validity. To determine construct validity, Spearman's correlations were calculated between the WHOQOL-BREF and the EuroQol-five-dimension-3-level questionnaire, the Health Utility Index Mark 2 and 3, the Hospital Anxiety and Depression Scale and the Impact of Event Scale. Discriminant validity between patients with minor injuries (i.e. Injury Severity Score (ISS)≤8) and moderate/severe injuries (i.e. ISS≥9) was examined by conducting Mann-Whitney *U* tests.

Results: In total, 202 patients (median 63y) participated in this study with a median of 32 days (interquartile range 29–37) post-trauma. The WHOQOL-BREF showed no problematic floor and ceiling effects. The CFA revealed a moderate model fit. The domains showed good internal consistency, with the exception of the social domain. All individual items and domain scores of the WHOQOL-BREF showed nearly symmetrical distributions since mean scores were close to median scores, except of the *'general health'* item. The highest percentage of missing values was found on the *'sexual activity'* item (i.e. 19.3%). The WHOQOL-BREF showed moderate construct and discriminant validity since in both cases, 67% of the hypotheses were confirmed.

Conclusion: The present study provides support for using the WHOQOL-BREF for the hospitalized trauma population since the questionnaire appears to be valid and reliable. The WHOQOL-BREF can be used to assess QoL in a heterogeneous group of hospitalized trauma patients accurately.

Trail registration: ClinicalTrials.gov identifier: NCT02508675.

Keywords: Injury, trauma, Quality of Life, validity, QoL questionnaire, WHOQOL-BREF

INTRODUCTION

According to the World Health Organization (WHO), trauma is a major and worldwide problem (1). It is increasingly important to focus on patient-centered outcomes in order to improve non-fatal outcome. Quality of Life (QoL) is a multidimensional concept including both positive and negative aspects of life and it incorporates a person's physical health, psychological state, level of independence, social relationships, personal beliefs and relationship to salient features of the environment (2). QoL measures patient's evaluation of functioning in line with their expectations.

The World Health Organization Quality of Life questionnaire (WHOQOL) provides a detailed assessment of each individual facet that is related to QoL. Currently, the WHOQOL is an internationally applicable, cross-culturally comparable and generic instrument for the assessment of QoL (3). The original WHOQOL was created by the WHOQOL Group in 1995 and consists of 100 items (3). Following the development of the WHOQOL-100, the WHOQOL Group developed an abbreviated form, i.e. the Abbreviated World Health Organization Quality of Life (WHOQOL-BREF) (2). The WHOQOL-BREF consists of 26 questions; one item for each of the 24 facets contained in the original WHOQOL-100 and two items concerning the 'overall QoL' and 'general health' (2, 4). The WHOQOL-BREF is very popular since its brevity reduces participant response burden and thus facilitates its use in conjunction with other measures (2).

In the general population, the WHOQOL-BREF is a valid and reliable measure for the assessment of QoL (2, 4). Several studies have validated the WHOQOL-BREF in specific subgroups of the population (5-11). In addition, the WHOQOL-BREF has also been validated in various patient groups (12-18).

The WHOQOL-BREF has been used to determine QoL for the trauma population (19-23); however, its methodological qualities in this population are unknown. Several studies have investigated the psychometric properties of the WHOQOL-BREF in specific subgroups of trauma patients (19-21). A previous study evaluated and defined reference values of the WHOQOL-BREF for patients with acetabular fractures (24). Although the WHOQOL-BREF was not validated in this study, the authors concluded that the WHOQOL-BREF can be used to assess QoL. Furthermore, the WHOQOL-BREF has been found to be an appropriate and valid measure for the assessment of QoL in patients with traumatic brain injury (TBI) (25) and in patients with spinal cord injury (SCI) (26). In the study amongst SCI-patients, a comparison between outcomes of SCI-patients and non-SCI participants (i.e. participants free of any acute or chronic medical condition) was made in order to validate the WHOQOL-BREF; however, construct validity was not determined (26).

Hence, a complete picture of the validity and reliability of WHOQOL-BREF in the heterogeneous hospitalized trauma population is not available yet. The aim of this study was to investigate the validity and reliability of the WHOQOL-BREF for use in hospitalized trauma patients.

METHODS

Design and setting

This cross-sectional validation study was approved by the Ethics Committee Brabant (project number NL50258.028.14) and was conducted in a Level 1 and Level 2 trauma centre. The study

was performed in compliance with the Declaration of Helsinki. This study was part of the Brabant Injury Outcome Surveillance (BIOS) which is a large prospective cohort study focusing on the prevalence, recovery patterns and risk factors of non-fatal outcome and costs after trauma (27).

Participants

The WHOQOL-BREF was examined in a random sample of trauma patients who were included in the BIOS. In the BIOS, adult trauma patients who were seen at the emergency department (ED), were admitted to a ward or an intensive care unit (ICU) and survived to hospital discharge were eligible for inclusion. In the BIOS, both intentional and unintentional injuries and all types and severity of injuries were included. Patients for this validation study were recruited between April 2016 and November 2016 and were invited to participate at one month post-trauma. Patients with a pathological fracture, insufficient knowledge of the Dutch language or with no permanent address of residence were excluded. For this validation study, proxy informants were excluded as QoL-measures cannot reliably be obtained by proxy informants (28, 29).

Data collection

Demographic characteristics were extracted from the self-reported questionnaires and included age and gender. Injury related characteristics including the Abbreviated Injury Scale (AIS) (30) and the Injury Severity Score (ISS) (31) were extracted from the Brabant Trauma Registry Database.

WHOQOL-BREF

The WHOQOL-BREF was included in the patient questionnaire of the BIOS. The WHOQOL-BREF produces a QoL-profile which consists of four domain scores including the physical (7 items), psychological (6 items), social (3 items) and environmental (8 items) domain. Additionally, there are two general items that are examined separately: item 1 asks about individuals 'overall perception of QoL' and item 2 asks about individuals 'overall perception of general health' (32). All items are rated on a 5-point scale. The mean score of items within each domain is used to calculate the domain scores. Mean scores are multiplied by four in order to make domain scores and subsequently, scores for each domain range from 4 to 20. For the two general items the range of single scores also vary from 4 to 20. In order to make the interpretation of the domains and the individual items more easy, all scores were converted to 0–100 (32). According to the WHOQOL-guideline, the assessment is discarded when <20% of the data is missing. Where an item is missing, the mean of other items in the domain was substituted. When ≥2 items are missing from the domain, the domain score cannot be calculated, with the exception of domain 3, where the domain score should only be calculated if ≤1 item is missing (32). Almost all items and domain scores are scaled in a positive direction (i.e. higher scores denote higher QoL), except for the items 'pain and discomfort', 'negative feelings' and 'dependence on medication or treatments' which are negatively framed. However, when domain scores are calculated, these negatively framed questions are transformed in positively framed questions.

Questionnaires for the validation of the WHOQOL-BREF

To determine the construct and discriminant validity of the WHOQOL-BREF, the random sample of patients completed the set of questionnaires after their written informed consent was obtained. The set of questionnaires to determine construct validity included the Impact of Event Scale (IES) (33) to measure symptoms of post-traumatic stress disorder (PTSD), the Hospital Anxiety and Depression Scale (HADS) (34) to screen for anxiety and depression, and

the EuroQol-five-dimension-3-level (EQ-5D-3L) (35) and the Health Utility Index Mark 2 and 3 (HUI2 and HUI3) (36) to measure HRQoL. See the protocol paper of the BIOS (27) for an overview of methodologic qualities of the measurements.

Statistical analyses

χ^2-tests and t-tests (and non-parametric tests for non-normal distributed data) were conducted to examine the difference in composition between the group of responders and non-responders regarding demographic and injury-related characteristics.

The percentage of missing values for each domain and the distribution of minimum and maximum possible domain scores (i.e. floor and ceiling effects) were calculated for the WHOQOL-BREF. Floor and ceiling effects were considered to be present if >15% of the respondents achieved the lowest or highest possible score (37).

A confirmatory factor analysis (CFA) was conducted to test whether the four-domain structure of the WHOQOL-BREF was suited to the hospitalized trauma population. For each of the four latent variables (i.e. physical, psychological, social and environmental domain), one factor loading was fixed to 1 (see **Appendix 7.A**) in order to achieve model identification. The maximum likelihood method was used to estimate the association between the items and the sub domains (i.e. latent factors). Goodness-of-fit was verified by the following fit indices: the Tucker-Lewis Index (TLI; recommended >0.95), Comparative Fit Index (CFI; recommended >0.95) and the Root Mean Square Error of Approximation (RMSEA; recommended <0.08) (38).

Reliability of the WHOQOL-BREF was examined by using Cronbach's alpha (CA) to test for internal consistency. Internal consistency indicates the correlation between a respondents' item-responses and suggests whether or not these items seem to measure the same construct (39). The CA was calculated for each sub domain separately. A coefficient of 0.70–0.80 indicates fair internal consistency, 0.80–0.90 indicates good internal consistency and ≥0.90 indicates excellent internal consistency (40). However, a CA >0.95 can indicate that the instrument contains too many items that are assessing the same underlying construct (41).

Due to non-normal distributions, validity of the WHOQOL-BREF was calculated using Spearman's correlation coefficient (r_s). Inter-item correlations were calculated for the two general items of the WHOQOL-BREF and the four subdomains. Correlation coefficients were calculated between the WHOQOL-BREF overall items and domain scores and the EQ-5D-3L, EQ-VAS, HUI2, HUI3, IES and HADS.

Construct validity estimates the degree to which the scores of the instrument are consistent with the hypotheses based on the assumption that the instrument measures the construct to be measured (42). There is no consensus on the number of hypotheses that should be tested, nor on the number of hypotheses that should be confirmed to ensure adequate construct validity. However according to the literature, 75% of the hypotheses should be confirmed to indicate good validity (43). There is moderate construct validity if 50–74% of the hypotheses are confirmed and poor construct validity is found if ≤49% of the hypotheses are confirmed (43).

Correlations with instruments measuring similar constructs should be ≥0.50 (i.e. high correlation) (44), indicating convergent validity (45). Correlations with instruments measuring related but

dissimilar constructs should be lower, i.e. 0.30-0.50 (i.e. moderate correlation) (44), which also indicate convergent validity (45). Correlations with instruments measuring unrelated constructs should be <0.30 (i.e. low correlation) (44), which indicates divergent validity (45). Correlations with instruments measuring related but dissimilar constructs should differ by a minimum of 0.10 from correlations with instruments measuring unrelated constructs (44). A valid questionnaire should show both convergent and divergent validity (46).

QoL is a broad concept. We hypothesized that convergent validity would be observed in the majority of the cases when construct validity was examined (see **Appendix 7.B**). We only expected to find divergent validity between the social domain of the WHOQOL-BREF and all HRQoL-measures, between the environmental domain and all HRQoL and psychological measures, between the psychological domain and the HUI2 and HUI3, between the 'overall QoL' item and the IES, and between the physical domain and the IES.

Another way to test the construct validity of a questionnaire is to examine the discriminant validity (or known-groups validity). For this, the instrument should be administered in two groups that are known to have or that logically should have different levels of the construct to confirm whether the hypothesized difference is reflected in the scores of the two groups (47). Discriminant validity of the WHOQOL-BREF between patients with minor injuries (i.e. ISS≤8) and patients with moderate/severe injuries (i.e. ISS≥9) was evaluated by conducting t-tests or Mann-Whitney *U* tests in non-normally distributed data. We hypothesized that patients with minor injuries have significantly higher scores compared to patients with moderate or severe injuries on the two general questions, the physical domain and the psychological domain of the WHOQOL-BREF (see **Appendix 7.C**). We further hypothesized to find no statistically significant differences on the social and environmental domain of the WHOQOL-BREF in patients with minor or with moderate/severe injuries.

Statistical test results were tested two-tailed and considered significant at the $p<0.05$ level. Except of the CFA, all analyses were conducted using SPSS V.24 (Statistical Package for Social Sciences, Chicago, Illinois, USA). CFA was performed by using Analysis of Moment Structures (AMOS) V.25.0.0 statistical software package.

RESULTS

General characteristics of the participants

During the inclusion period, 768 patients were randomly selected for the validation study and fulfilled the inclusion criteria. Of those patients, 10 died within the first month post-trauma. In total, 202 patients (26% response rate) agreed to participate.

The age of the participants ranged from 18 to 94 years with a median age of 63 (**Table 1**). More than half (56.5%) of the participants was male. Compared to the non-responders, responders were significantly more likely to be male, to be younger and to have a higher injury severity as measured by the ISS. Responders had a significantly longer length of hospital stay and were significantly more frequently admitted to an ICU. The median time of completing the WHOQOL-BREF was 32 days (interquartile range 29–37).

Table 1: Demographic characteristics of the responders and non-responders of the validation study

	Responder (n=202), n	Non-responders (n=566), n	p-values
Gender (male)	108 (53.5%)	246 (43.5%)	χ^2: p=0.011
Missing	0 (0%)	0 (0%)	
Age (yrs)	Median 63 (IQR 53–76)	Median 69 (IQR 47–83)	Mann-Whitney *U*: p=0.078
18–24	7 (3.5%)	38 (6.7%)	
25–44	27 (13.4%)	89 (15.7%)	
45–64	72 (35.6%)	125 (22.1%)	
65–74	41 (20.3%)	66 (11.7%)	
75–84	35 (17.3%)	124 (21.9%)	
85+	20 (9.9%)	124 (21.9%)	
Missing	0 (0%)	0 (0%)	
Days admitted to hospital	Median 5.5 (IQR 3–11)	Median 4 (IQR 2–10)	Mann-Whitney *U*: p=0.017
≤2	38 (18.8%)	150 (26.5%)	
3-7	70 (34.7%)	184 (32.5%)	
8-14	43 (21.3%)	123 (21.7%)	
≥15	25 (12.4%)	44 (7.8%)	
Missing	26 (12.9%)	65 (11.5%)	
Injury severity (ISS)	Median 9 (IQR 4–10)	Median 5 (IQR 3–9)	Mann-Whitney *U*: p=0.000
ISS 1–3	24 (11.9%)	130 (23%)	
ISS 4–8	56 (27.7%)	181 (32%)	
ISS 9–15	70 (34.7%)	174 (30.7%)	
ISS 16+	26 (12.9.8%)	16 (2.8%)	
Missing	26 (12.9%)	65 (11.5%)	
ICU-admission (yes)	28 (13.9%)	21 (3.7%)	χ^2: p=0.000
Missing	0 (0%)	0 (0%)	

Abbreviations: ICU, intensive care unit; ISS, Injury Severity Score; IQR, Interquartile range; yrs,years.

Descriptive statistics

At one month post-trauma, the average domain score (range 0–100) was 55 for the physical, 70 for the psychological, 73 for the social and for the environmental domain (**Table 2**). For each domain score and for the 'overall QoL' item, the median was relatively close to the mean indicating that distributions were nearly symmetrical. However, the 'general health' item revealed a large difference between the mean and the median score (mean=60, median=75). No floor effects were observed for the domains. However, for the two general items this was 2.3% and 3.4%, respectively. For the domain scores, percentages of the ceiling effects varied from 1.1% for the physical domain to 10.2% for the social domain. For the two general items, the ceiling effects were 23.3% and 13.0%, respectively.

For all individual items of the domains of the WHOQOL-BREF, mean scores were close to the median scores. The item *'How satisfied are you with the support you get from your friends?*' showed the highest outcome (mean=4.27, SD=0.76). This item also showed the lowest percentage of floor value (0.6%). The item *'How satisfied are you with your capacity for work?'* showed the lowest outcome (mean=2.69, SD=1.13) and showed the highest percentage

of floor value (15.7%). The item *'How satisfied are you with your ability to perform your daily living activities?'* (mean=2.79, SD=1.06) revealed the fewest percentage of ceiling value (4.5%). The items *'How healthy is your physical environment?'* and *'Are you able to accept your bodily appearance?'* showed the highest percentage of ceiling values (both 46.9%). The item 'sexual activity' had the highest percentage of missing values (19.3%) (**Table 2**).

Table 2: Missing items and score distributions for the individual items (range 1–5), two general items and domain scores (range 0–100) of the WHOQOL-BREF

Domains and items	n	n (%) missing	Mean (SD)	Median (IQR)	Floor effects, n (%)	Ceiling effects, n (%)
General items						
1. How would you rate your quality of life?	**176**	**26 (12.9)**	**71 (24)**	**75 (50-75)**	**4 (2.3)**	**41 (23.3)**
2. How satisfied are you with your health?	**177**	**25 (12.4)**	**60 (26)**	**75 (50-75)**	**6 (3.4)**	**23 (13.0)**
Physical domain	**174**	**28 (13.9)**	**55 (20)**	**54 (39-68)**	**0 (0)**	**2 (1.1)**
1. How satisfied are you with your ability to perform your daily living activities?	177	25 (12.4)	2.79 (1.06)	3 (2-4)	18 (10.2)	8 (4.5)
2. How much do you need any medical treatment to function in your daily life?	175	27 (13.4)	3.45 (1.23)	3 (3-5)	13 (7.4)	47 (26.9)
3. Do you have enough energy for everyday life?	176	26 (12.9)	3.61 (1.06)	4 (3-4)	7 (4.0)	40 (22.7)
4. How well are you able to get around?	177	25 (12.4)	3.25 (1.28)	3 (2-4)	17 (9.6)	34 (19.2)
5. To what extent do you feel that physical pain prevents you from doing what you need to do?	177	25 (12.4)	3.31 (1.08)	3 (3-4)	7 (4.0)	28 (15.8)
6. How satisfied are you with your sleep?	177	25 (12.4)	3.27 (1.11)	3 (2-4)	9 (5.1)	26 (14.7)
7. How satisfied are you with your capacity for work?	172	30 (14.9)	2.69 (1.12)	3 (2-4)	27 (15.7)	9 (5.2)
Psychological domain	**173**	**29 (14.4)**	**70 (19)**	**71 (58-83)**	**0 (0)**	**6 (3.5)**
1. Are you able to accept your bodily appearance?	177	25 (12.4)	4.18 (0.93)	4 (4-5)	2 (1.1)	83 (46.9)
2. How often do you have negative feelings such as blue mood, despair, anxiety, depression?	177	25 (12.4)	3.86 (1.04)	4 (3-5)	3 (1.7)	58 (32.8)
3. How much do you enjoy life?	173	29 (14.4)	3.50 (0.93)	4 (3-4)	7 (4.0)	20 (11.6)
4. How satisfied are you with yourself?	175	27 (13.4)	3.69 (1.00)	4 (3-4)	8 (4.6)	34 (19.4)
5. To what extent do you feel your life to be meaningful?	173	29 (14.4)	3.69 (0.95)	4 (3-4)	5 (2.9)	32 (18.5)
6. How well are you able to concentrate?	177	25 (12.4)	3.79 (1.03)	4 (3-5)	3 (1.7)	53 (29.9)

Table 2 *(continued)*

Domains and items	n	n (%) missing	Mean (SD)	Median (IQR)	Floor effects, n (%)	Ceiling effects, n (%)
Social domain	**176**	**26 (12.9)**	**73 (18)**	**75 (64-83)**	**0 (0)**	**18 (10.2)**
1. How satisfied are you with your personal relationships?	175	27 (13.4)	4.19 (0.83)	4 (4-5)	3 (1.7)	67 (38.3)
2. How satisfied are you with the support you get from your friends?	176	26 (12.9)	4.27 (0.76)	4 (4-5)	1 (0.6)	74 (42.0)
3. How satisfied are you with your sex life?	163	39 (19.3)	3.27 (1.08)	3 (3-4)	14 (8.6)	21 (12.9)
Environmental domain	**176**	**26 (12.9)**	**73 (18)**	**75 (63-88)**	**0 (0)**	**9 (5.1)**
1. Have you enough money to meet your needs?	177	25 (12.4)	3.97 (1.01)	4 (3-5)	3 (1.7)	72 (40.7)
2. How safe do you feel in your daily life?	176	23 (12.9)	4.10 (0.96)	4 (3-5)	3 (1.7)	76 (43.2)
3. How satisfied are you with your access to health services?	176	26 (12.9)	3.86 (0.89)	4 (3-4)	3 (1.7)	43 (24.4)
4. How satisfied are you with the conditions of your living place?	175	27 (13.4)	3.98 (0.97)	4 (4-5)	6 (3.4)	55 (31.4)
5. How available to you is the information that you need in your day-to-day life?	175	27 (13.4)	4.06 (0.98)	4 (3-5)	5 (2.9)	72 (41.1)
6. To what extent do you have the opportunity for leisure activities?	174	28 (13.9)	3.55 (1.27)	4 (3-5)	16 (9.2)	50 (28.7)
7. How healthy is your physical environment?	175	27 (13.4)	4.25 (0.82)	4 (4-5)	4 (2.3)	82 (46.9)
8. How satisfied are you with your transport?	175	27 (13.4)	3.74 (1.13)	4 (3-5)	9 (5.1)	51 (29.1)

Abbreviations: QoL, Quality of Life; SD, Standard Deviation; IQR, Interquartile range.

Inter-correlations of the WHOQOL-BREF

As shown in **Table 3**, statistically significant inter-item correlations were found. The highest correlation was found between the psychological domain and the environmental domain (r_s=0.644, p<0.01). The lowest correlation was found between the physical domain and social domain of the WHOQOL-BREF (r_s=0.225, p<0.01).

Table 3: Spearman correlations between the WHOQOL-BREF domains and with the two general items

Domain/item	'Overall QoL' item	'General health' item	Physical domain	Psychological domain	Social domain	Environmental domain
	r_s	r_s	r_s	r_s	r_s	r_s
'Overall QoL' item	1	0.621**	0.535**	0.639**	0.362**	0.534**
'General health' item	0.621**	1	0.633**	0.556**	0.298**	0.454**
Physical domain	0.535**	0.633**	1	0.520**	0.225**	0.539**
Psychological domain	0.639**	0.556**	0.520**	1	0.452**	0.644**
Social domain	0.362**	0.298**	0.225**	0.452**	1	0.616**
Environmental domain	0.534**	0.454**	0.539**	0.644**	0.616**	1

**p<0.01, two–tailed

Abbreviations: QoL, Quality of Life; r_s, Spearman's correlation coefficient.

Confirmatory factor analysis

To test how well the items of the WHOQOL-BREF represents the number of constructs (i.e. domains), a CFA was conducted. **Table 4** shows the standardized regression weights for the 24 facets of the WHOQOL-BREF for the 142 patients who completed all items of the questionnaire. Inspection of the parameter estimates revealed that on the physical domain, the items *'How satisfied are you with your ability to perform your daily living activities?'* and *'How satisfied are you with your capacity for work?'* had the highest loadings on the corresponding latent factor (i.e. variable which is not directly observable and is assumed to affect the response variable). With regard to the psychological, social and environmental domain, the highest loadings were found, respectively, for items *'How much do you enjoy life?'*, *'How satisfied are you with your personal relationships?'* and *'How satisfied are you with the conditions of your living place?'*. Somewhat lower factor loadings on the physical domain were found for the items *'How much do you need any medical treatment to function in your daily life?'* and *'How satisfied are you with your sleep?'* (0.447 and -0.477 respectively). Besides, a lower factor loading was found for the item *'How healthy is your physical environment?'* (0.479) on the environmental domain.

TLI was 0.781, the CFI was 0.805 and the RMSEA was 0.095 which indicates a moderate model fit.

Table 4: Standardized regression weights of the facets on their latent variables (i.e. domains): four-domain model (n=142)

Domains	Items	I	II	III	IV
I Physical domain	1. How satisfied are you with your ability to perform your daily living activities?	-0.868*			
	2. How much do you need any medical treatment to function in your daily life?	0.447*			
	3. Do you have enough energy for everyday life?	-0.638*			
	4. How well are you able to get around?	-0.651*			
	5. To what extent do you feel that physical pain prevents you from doing what you need to do?	0.541*			
	6. How satisfied are you with your sleep?	-0.477*			
	7. How satisfied are you with your capacity for work?	-0.843*			

Table 4 *(continued)*

Domains	Items	I	II	III	IV
II Psychological domain	1. Are you able to accept your bodily appearance?		0.694*		
	2. How often do you have negative feelings such as blue mood, despair, anxiety, depression?		-0.575*		
	3. How much do you enjoy life?		0.843*		
	4. How satisfied are you with yourself?		0.776*		
	5. To what extent do you feel your life to be meaningful?		0.762*		
	6. How well are you able to concentrate?		0.592*		
III Social domain	1. How satisfied are you with your personal relationships?			0.788*	
	2. How satisfied are you with the support you get from your friends?			0.684*	
	3. How satisfied are you with your sex life?			0.574*	
IV Environmental domain	1. Have you enough money to meet your needs?				0.518*
	2. How safe do you feel in your daily life?				0.658*
	3. How satisfied are you with your access to health services?				0.679*
	4. How satisfied are you with the conditions of your living place?				0.779*
	5. How available to you is the information that you need in your day-to-day life?				0.664*
	6. To what extent do you have the opportunity for leisure activities?				0.601*
	7. How healthy is your physical environment?				0.479*
	8. How satisfied are you with your transport?				0.685*

*p–value <0.001

Internal consistency

The CA's of the physical, psychological and environmental domains were ≥0.80 indicating good internal consistency of the particular items within the these domains (**Table 5**). However for the social domain, the CA was <0.70 indicating low internal consistency.

Table 5: Internal consistency of the domain scores of the WHOQOL-BREF

Domains	n	Cronbach's alpha
Physical domain	167	0.838
Psychological domain	168	0.860
Social domain	160	0.675
Environmental domain	165	0.849

Construct validity

Spearman's correlation coefficients between the WHOQOL-BREF and the HRQoL and psychological measures were almost all statistically significant (**Table 6**).

The scores for the two general questions and the physical, psychological, social and environmental domains were all positively correlated with patients' self-reported HRQoL. Of all HRQoL measures, the lowest correlation was found between the social domain of the WHOQOL-BREF and the EQ-VAS (r_s=0.139, not significant). The highest correlation was found between the physical domain and the EQ-VAS (r_s=0.674, p<0.01).

Significant inverse correlations were found between the WHOQOL-BREF and the psychological measures with the psychological domain presenting the strongest inverse correlation with the HADSD (r_s=-0.656, p<0.01). The lowest correlation was found between the social domain and the IES (r=-0.232, p<0.01). Negative coefficients indicate that higher HADS and IES-scores (i.e. the higher the symptoms of anxiety, depression or PTSD) are related to worse/lower QoL-domain scores.

To determine construct validity, 42 hypotheses were created to indicate the convergent and divergent validity of the WHOQOL-BREF (see **Appendix 7.B**). Of these hypotheses, 28 (67%) were confirmed. Contrary to our hypotheses, convergent validity was found for the environmental domain of the WHOQOL-BREF with all HRQoL (range r_s=0.389–0.456, all p<0.01) and psychological instruments (range r_s=-0.357–-0.521, all p<0.01). In addition, convergent validity was found between the psychological domain and the HUI2 and HUI3 whereas we hypothesized to find divergent validity (r_s=0.401 and r_s=0.449 respectively and both p<0.01). We hypothesized to find divergent validity between the 'overall QoL' item and the IES. However, results revealed convergent validity (r_s=-0.331, p<0.01). Last, moderate correlations were hypothesized between the social domain and the HADSA, between the 'general health' item and the IES, between the psychological domain and the IES and between the social domain and the IES. Though, all these correlations were low (r_s=-0.276, r_s=-0.287, r_s=-0.475 and r_s=-0.232, respectively and all p<0.01) (see **Appendix 7.B** for more details).

Table 6: Spearman correlations between the WHOQOL-BREF and the mean EQ-5D-3L, EQ-VAS, HUI Mark 2, HUI Mark 3, HADS and IES

Domain/items	HRQoL measures				Psychological measures		
	EQ-5D-3L	EQ-VAS	HUI2	HUI3	HADSA	HADSD	IES
	r_s	r_s	r_s	r_s	r_s	r_s	r_s
'Overall QoL' item	0.499**	0.499**	0.420**	0.487**	-0.502**	-0.580**	-0.331**
'General health' item	0.479**	0.628**	0.524**	0.548**	-0.397**	-0.520**	-0.287**
Physical domain	0.662**	0.674**	0.669**	0.657**	-0.457**	-0.654**	-0.321**
Psychological domain	0.438**	0.461**	0.401**	0.449**	-0.642**	-0.656**	-0.475**
Social domain	0.213**	0.139 (NS)	0.173*	0.146 (NS)	-0.276**	-0.345**	-0.232**
Environmental domain	0.456**	0.402**	0.389**	0.412**	-0.517**	-0.521**	-0.357**

*p<0.05, two–tailed
**p<0.01, two–tailed
Abbreviations: NS, not significant; EQ–5D–3l, EuroQol–five–dimension–3–level; EQ–VAS, EuroQoL Visual Analogue Scale; HUI2, Health Utility Index Mark 2; HUI3, Health Utility Index Mark 3; HADSA, Hospital Anxiety and Depression Scale subscale anxiety; HADSD, Hospital Anxiety and Depression Scale subscale depression; IES, Impact of Event Scale; r_s, Spearman's correlation coefficient; QoL, Quality of Life.

Discriminant validity

Six hypothesis were created to evaluate discriminant validity (see **Appendix 7.C**). Of these hypotheses, 4 (67%) were confirmed indicating moderate discriminant validity. Hospitalized trauma patients with minor injuries revealed higher (i.e. better) scores on the 'overall QoL' item and on the psychological domain compared to those with moderate or severe injuries (**Table 7**). However, these results were not statically significant and therefore, these findings reject our hypothesis. As hypothesized, hospitalized trauma patients with minor injury showed significantly higher scores on the 'general health' item and on the physical domain. No statistically significant differences were identified between the social and environmental domain of the WHOQOL-BREF between patients with minor or with moderate/severe injuries, which is also in line with our hypotheses.

Table 7: Discriminant validity of the WHOQOL-BREF between patients with minor injury (i.e. ISS≤8) (n=91) and patients with moderate/severe injury (i.e. ISS≥9) (n=86)

Domains/items	Minor injury (ISS≤8)	Moderate/severe injury (ISS≥9)	p-value*
	Median (IQR)	Median (IQR)	
'Overall QoL' item	75 (75–100)	75 (50–75)	0.063
'General health' item	75 (50–75)	50 (25–75)	0.033
Physical domain	61 (43–71)	50 (39–64)	0.046
Psychological domain	75 (63–83)	71 (54–83)	0.217
Social domain	75 (67–83)	75 (63–83)	0.899
Environmental domain	75 (63–88)	75 (63–88)	0.794

*calculated with Mann–Whitney *U* test.

Abbreviations: SD, Standard Deviation; ISS, Injury Severity Score; IQR, Interquartile range; QoL, Quality of Life.

DISCUSSION

This is the first study that examined the validity and reliability of the WHOQOL-BREF for the whole hospitalized trauma population. It is important to measure QoL as a complementary outcome measure in trauma survivors. In general, the results support the validity of the WHOQOL-BREF. The questionnaire showed no problematic floor and ceiling effects, symmetrical distributions and the CFA revealed a moderate model fit. Overall, the WHOQOL-BREF showed good internal consistency and moderate construct and discriminant validity in the clinical trauma population.

The lowest domain score is found on the physical domain. This indicates that at one month post-trauma, hospitalized trauma patients generally have a relatively low activity level, a greater dependence on medicinal substances and medical aids, insufficient energy and mobility, more pain and discomfort, a lack of sufficient sleep and rest and low work capacity. This outcome is in agreement with the literature in which patients with spinal cord injury and patients with a cataract also reported the lowest domain score on the physical domain (18, 26).

We found nearly symmetric distributions of the first general item (i.e. 'overall QoL') and all sub domain scores of the WHOQOL-BREF, except for the second general item (i.e. 'general health'). Interestingly, these results imply that patients who are not satisfied with their health condition, can report a high QoL. Except of the 'overall QoL' item, all sub domains of the WHOQOL-BREF have acceptable floor and ceiling effects. This outcome is in line with the literature (25, 26, 48).

For all sub domains measured at one month post-trauma, no floor effects were identified. Conversely, the two general items (i.e. 'overall QoL' and 'general health') did show floor effects. This can be explained since a trauma is a sudden life event, which can have a large impact on patients' life (49). In line with previous studies (25, 26, 48, 50), the sexuality item had the highest missing rate value.

The Cronbach's alpha's of almost all sub domains were good indicating good reliability, except for the social domain. Previous validation studies also found a low CA for the social domain (4, 12, 15, 25, 26, 51, 52), except of one study amongst medical students (5). An explanation for this is that the social domain includes only three items whereas the other domains include 6–8 items. The CA is generally lower if a scale contains only few items (53).

Generally, moderate to high correlations were found between the WHOQOL-BREF and questionnaires measuring similar concepts. Low correlations were found in questionnaires measuring dissimilar concepts. QoL increases when HRQoL increases in which the physical domain correlated most strongly with the HRQoL-measures. Furthermore, QoL decreases in relation to symptoms of anxiety, depression or PTSD. These results are comparable to the results of other studies validating the WHOQOL-BREF (11, 12, 54-58). Findings indicate that the psychological domain of the WHOQOL-BREF measures more depressive instead of anxiety symptoms. This indicates that QoL is associated with depressive symptoms and this also has been confirmed in earlier studies (54, 56, 58-62). Moreover, psychological complaints seem to be an important and underestimated risk factor for a decreased QoL among trauma patients (22). Overall, low or moderate correlations were found between the IES and the general items and domains of the WHOQOL-BREF. Previous studies amongst trauma patients showed that PTSD was significantly associated with low scores on the WHOQOL-BREF (20, 23).

The correlation coefficients between the environmental domain and the HRQoL and psychological instruments were larger than we hypothesized. Earlier research found moderate correlations between functional outcomes and the environmental domain (15, 55). In hindsight, our method of reasoning for the hypotheses of this sub domain might have been incorrect since the environmental domain compromise items such as *'To what extent do you have the opportunity for leisure activities?'* and *'How safe do you feel in your daily life?'*. These items are more highly related to HRQoL and psychological functioning than we expected.

Results from the discriminant analysis revealed that the WHOQOL-BREF is moderately able to discriminate between patients with minor injuries and patients with moderate or severe injuries. Two previous studies found good discriminant validity regarding different severity levels of patients with a depression or patients with HIV (56, 57).

A strength of this study is that we had a relatively large sample size, compared to previous validation studies of the WHOQOL-BREF (14-16, 24, 26, 56-58). Additionally, we included various measures to determine construct and discriminant validity. However, the low response rate reduces the generalizability of the study findings. In addition, a high percentage of missing items on the WHOQOL-BREF was found. A reason for this might be that the data of this validation study was collected alongside a large prospective cohort study (27) in which a comprehensive set of questionnaires needs to be completed by patients. Because of the large number of questions, patients might have more easily neglected or overlooked certain questions.

The WHOQOL-BREF might be a useful tool to optimize trauma care because of the included questions about patients' satisfaction with functioning. The questionnaire makes it easy to identify issues that patients have to deal with after their trauma. The CFA showed moderate model fit which can be explained by the small sample size of patients (n=142). Future studies should further examine the psychometric properties of the WHOQOL-BREF in a larger sample of hospitalized adult trauma patients. For instance, by testing the test-retest reliability and by providing a more precise insight about the four-domain structure of the WHOQOL-BREF.

CONCLUSIONS

The validity and reliability of the WHOQOL-BREF for the hospitalized trauma population were not examined yet. The present study provides support for using the WHOQOL-BREF for the hospitalized trauma population since the questionnaire appears to be valid and reliable. For that reason, the WHOQOL-BREF can be used to assess QoL in hospitalized trauma patients in an accurate way.

ACKNOWLEDGEMENTS

We would like to thank all members of the BIOS-group who gave valuable time effort and support in order to collect data in a comprehensive group of trauma patients.

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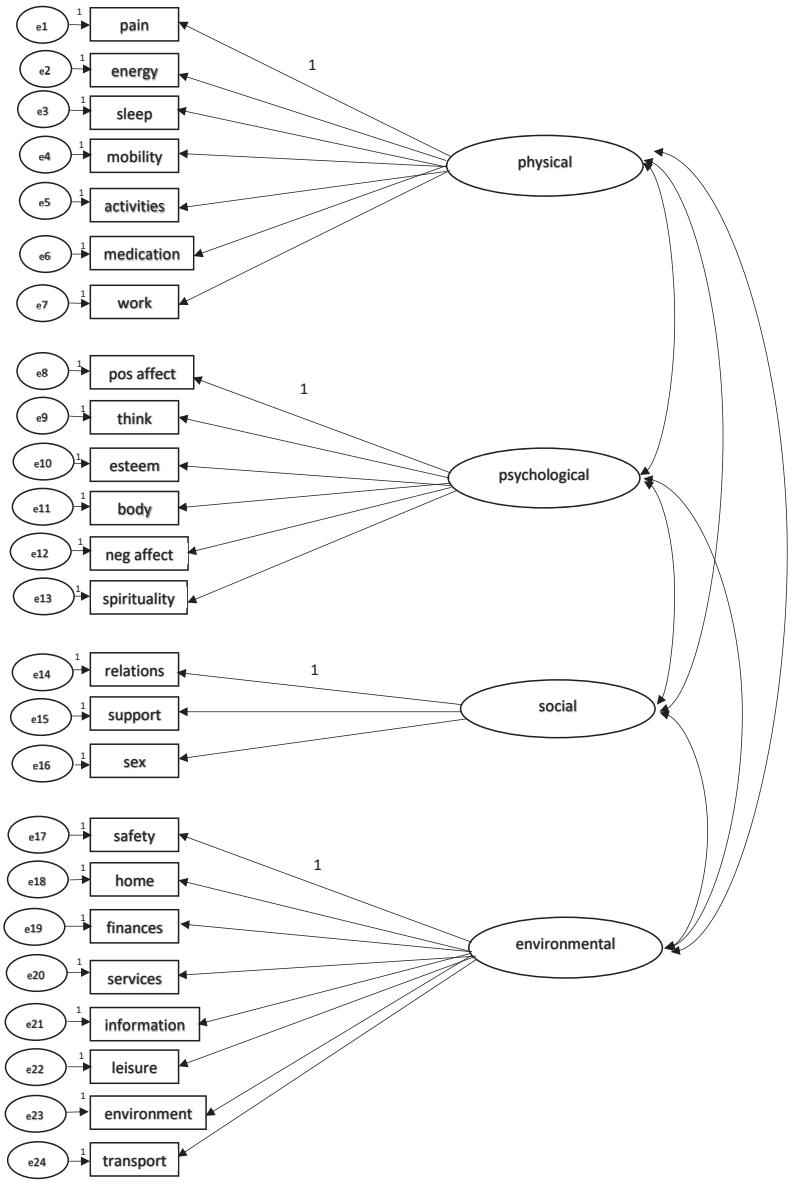
APPENDICES

Appendix 7.A: Hypothesized factor model



Appendix 7.B

Table 1: Hypothesis testing of the construct validity of the WHOQOL-BREF and HRQoL-measures

	EQ-5D-3L			EQ-VAS			HUI2			HUI3		
	r_s	Hypothesis testing		r_s	Hypothesis testing		r_s	Hypothesis testing		r_s	Hypothesis testing	
		Hypothesis	Outcome		Hypothesis	Outcome		Hypothesis	Outcome		Hypothesis	Outcome
'Overall QoL' item	0.499**	r_s: ≥0.30	Confirmed	0.499**	r_s: ≥0.30	Confirmed	0.420**	r_s: ≥0.30	Confirmed	0.487**	r_s: ≥0.30	Confirmed
'General health' item	0.479**	r_s: ≥0.30	Confirmed	0.628**	r_s: ≥0.30	Confirmed	0.524**	r_s: ≥0.30	Confirmed	0.548**	r_s: ≥0.30	Confirmed
Physical domain	0.662**	r_s: ≥0.30	Confirmed	0.674**	r_s: ≥0.30	Confirmed	0.669**	r_s: ≥0.30	Confirmed	0.657**	r_s: ≥0.30	Confirmed
Psychological domain	0.438**	r_s: ≥0.30	Confirmed	0.461**	r_s: ≥0.30	Confirmed	0.401**	r_s: 0.10–0.29	Not confirmed	0.449**	r_s: 0.10–0.29	Not confirmed
Social domain	0.213**	r_s: 0.10–0.29	Confirmed	0.139 (NS)	r_s: 0.10–0.29	Confirmed	0.173*	r_s: 0.10–0.29	Confirmed	0.146 (NS)	r_s: 0.10–0.29	Confirmed
Environmental domain	0.456**	r_s: 0.10–0.29	Not confirmed	0.402**	r_s: 0.10–0.29	Not confirmed	0.389**	r_s: 0.10–0.29	Not confirmed	0.412**	r_s: 0.10–0.29	Not confirmed

Abbreviations: NS, not significant; EQ–5D–3l, EuroQol–five–dimension–3–level; EQ–VAS, EuroQoL Visual Analogue Scale; HUI2, Health Utility Index Mark 2; HUI3, Health Utility Index Mark 3; r_s, Spearman's correlation coefficient; QoL, Quality of Life; NS, not statistically significant.

Table 2: Hypothesis testing of the convergent and divergent validity of the WHOQOL-BREF and psychological measures

	HADSA			HADSD			IES		
	r_s	Hypothesis testing		r_s	Hypothesis testing		r_s	Hypothesis testing	
		Hypothesis	Outcome		Hypothesis	Outcome		Hypothesis	Outcome
'Overall QoL' item	-0.502**	r_s: ≥0.30	Confirmed	-0.580**	r_s: ≥0.30	Confirmed	-0.331**	r_s: 0.10–0.29	Not confirmed
'General health' item	-0.397**	r_s: ≥0.30	Confirmed	-0.520**	r_s: ≥0.30	Confirmed	-0.287**	r_s: ≥0.30	Not confirmed
Physical domain	-0.457**	r_s: ≥0.30	Confirmed	-0.654**	r_s: ≥0.30	Confirmed	-0.321**	r_s: 0.10–0.29	Confirmed
Psychological domain	-0.642**	r_s: ≥0.30	Confirmed	-0.656**	r_s: ≥0.30	Confirmed	-0.475**	r_s: ≥0.30	Not confirmed
Social domain	-0.276**	r_s: ≥0.30	Not confirmed	-0.345**	r_s: ≥0.30	Confirmed	-0.232**	r_s: ≥0.30	Not confirmed
Environmental domain	-0.517**	r_s: 0.10–0.29	Not confirmed	-0.521**	r_s: 0.10–0.29	Not confirmed	-0.357**	r_s: 0.10–0.29	Not confirmed

Abbreviations: HADSA, Hospital Anxiety and Depression Scale subscale anxiety; HADSD, Hospital Anxiety and Depression Scale subscale depression; IES, Impact of Event Scale; r_s, Spearman's correlation coefficient; QoL, Quality of Life.

Appendix 7.C

Table 1: Hypothesis testing of the discriminant validity of the WHOQOL-BREF

	Minor injury (ISS≤8)		Moderate/severe injury (ISS≥9)		p-value*	Hypothesis testing	
	n	Median (IQR)	n	Median (IQR)		Hypothesis	Outcome
'Overall QoL' item	88	75 (75-100)	86	75 (50-75)	0.063	Patients with minor injuries will have a statistically significant higher score on the 'Overall QoL' item compared to patients with moderate or severe injuries.	Not confirmed
'General health' item	89	75 (50-75)	86	50 (25-75)	0.033	Patients with minor injuries will have a statistically significant higher score on the 'General health' item compared to patients with moderate or severe injuries.	Confirmed
Physical domain	91	61 (43-71)	81	50 (39-64)	0.046	Patients with minor injuries will have a statistically significant higher score on the physical domain compared to patients with moderate or severe injuries.	Confirmed
Psychological domain	88	75 (63-83)	83	71 (54-83)	0.217	Patients with minor injuries will have a statistically significant higher score on the psychological domain compared to patients with moderate or severe injuries.	Not confirmed
Social domain	91	75 (67-83)	83	75 (63-83)	0.899	There is no statistically significant difference in scores between patients with minor or moderate/severe injuries on the social domain.	Confirmed
Environmental domain	91	75 (63-88)	83	75 (63-88)	0.794	There is no statistically significant difference in scores between patients with minor or moderate/severe injuries on the environmental domain.	Confirmed

*calculated with Mann–Whitney *U* test.

Abbreviations: SD, Standard Deviation; ISS, Injury Severity Score; IQR, Interquartile range; QoL, Quality of Life.

8

Chapter

General discussion

The aim of this thesis was to expand the knowledge on the prevalence, recovery patterns and determinants of non-fatal outcome after trauma. In this chapter, the applied methodology of the studies included in this thesis is discussed in the light of the current literature. In addition, the scientific and clinical implications as well as the implications for policy makers are addressed.

Methodological considerations

Substantial differences exist in methods to measure non-fatal outcome after trauma, including instruments, time assessments and length of follow-up (FU). Besides, previous studies focussed on specific sub groups of patients (e.g. severe trauma (1-6) or exclusion of elderly (7-10)). Subsequently, these variations limit the comparability between study results. The choices in the methodology of the conducted studies and their limitations should be taken into account when interpreting the results as presented in this thesis. In the following paragraphs, the internal and external validity of this thesis will be addressed.

Internal validity

Selection bias, information bias and confounding reduce the internal validity of a study (11, 12). Selection bias occurs due to the composition of the study population (11). Information bias refers to bias due to errors in the measurements (11). Confounding occurs when the observed association between an independent and dependent variable may be biased if it is mixed with those of one or more risk factors of the dependent variable which are associated with the independent variable as well (13). In longitudinal observational cohort studies, such as the Brabant Injury Outcome Surveillance (BIOS), response rates, loss to FU and confounding are important issues (14).

Selection bias

- *BIOS study*

Due to the unexpected nature of a trauma and the loss of control over patients' own situation, obtaining informed consent early after trauma is considered problematic (15). In the BIOS study, differences were identified between responders and non-responders (e.g. age, gender). Participation in a longitudinal cohort study is frequently correlated with cultural or lifestyle factors such as gender, marital status or residence in a particular region (14, 16), possibly inducing selection bias. It is well known that the lower the response rate, the higher the risk of a biased sample (17). For that reason, we tried to increase the response rate in the BIOS by allowing patients to flow in at each measure point up until 1 year post-trauma. In total, 50% of the total eligible population participated in the BIOS study. In *Chapter 5* and *7*, results were based on sub analyses of the BIOS study in which 31% and 26%, respectively, of the eligible population participated. An important limitation of the BIOS was the 18% response rate for the 1 week assessment, introducing a great risk of selection bias at this time point. In most cases, non-respondents of the 1 week assessment felt too disabled to respond or patients felt overwhelmed by their trauma and stated that it was too early to participate in the study. We tried to reduce loss to FU by using telephone reminders and by sending shortened questionnaires to patients who stated that it took too much time to complete the BIOS questionnaires. If too many participants are lossed to FU, differences in outcomes or conclusions can arise (18). In the BIOS study, patients aged 18-24 were most likely to be lossed to FU. However, previous studies also reported high loss-to-FU rates in younger patients (1, 19, 20). In addition, patients who recover completely are more likely to be lossed to FU. Although the BIOS study provides unique data, the selective non-response may have underestimated the adverse health effects very early after non-fatal trauma. In contrast, selective loss to FU of young and recovered patients may have led to an overestimation of the long-term adverse health effects after trauma.

The most common method for dealing with missing data is to exclude participants with missing data (i.e. complete case analysis) (21, 22). Nevertheless, this method has severe drawbacks since non-response is seldom at random. Subsequently, this reduces the generalizability of the study findings (21, 22). For the analyses of the BIOS study, multiple imputation (MI) was used. Although analyzing multiply imputed data sets is time consuming and requires statistical expertise (23), MI is a solid technique to improve the validity of clinical research if data is missing at random (21). Here, bias can be overcome since MI allows participants with incomplete data to be included in the analyses (21). Small or even no differences were identified between the means and standard deviations (SDs) of the original dataset of the BIOS and the means and SDs of the imputed dataset. However, considerable lower means and SDs were found in the imputed dataset of the Health Utilities Index Mark 2 and Mark 3 at 1 week post-trauma as well on the EuroQol-5D-3L at 12 months. In addition, the means and SDs in the imputed dataset of the Impact of Event Scale (IES) revealed higher outcomes as compared with the means and SDs of the original dataset. As compared with the orgingal dataset, males and females, patients aged 18-24 or aged 75-84, patients with low educational level and those with a very minor injury (i.e. Injury Severity Score 1-3), revealed slightly higher means and SDs of the health status (HS) measures as compared with the means and SDs of the imputed dataset.

- *Systematic review*

In the studies included in the systematic review on the effect of socio-economic status (SES) on non-fatal outcome after trauma, relevant characteristics of responders and non-responders were often not reported. Besides, there was a lack of an adequate description as well as clear reasons for loss to FU of the included studies. Therefore, it cannot be determined whether selection bias in the included studies has occurred or not.

- *Qualitative study*

In order to gain more insight into changes in perceived QoL after trauma, a focus group study was conducted in which only 26% of the eligible patients were willing to participate. Here, reported QoL might be underestimated since one out of five eligible patients either stated that a) their participation was too confrontational or b) they were unable to participate in the focus group because of their bad overall condition.

Information bias

- *BIOS study*

Measuring the psychological consequences after trauma is challenging, especially in large sample sizes. A clinical interview, which is considered as the 'gold standard' to diagnose anxiety, depression or post-traumatic stress (24, 25), was not feasible due to the large sample size of the BIOS study. Therefore, we used self-reported questionnaires to screen for psychological symptoms. For this purpose, we used the Hospital Anxiety and Depression Scale (HADS) and the IES. The HADS is one of the most frequently used screening instruments in medically ill patients (26-28) and the IES has been used in several studies focusing on non-fatal outcome after trauma (5, 29-33).

Results from self-reported questionnaires for psychological problems are sometimes hard to interpret, especially when different cut-off points are used in the literature. As compared with previous studies (34-38), we found lower prevalence rates of symptoms of post-traumatic stress, especially early post-trauma. This can be explained by the use of a relatively high cut-off point for

the IES in our study. We used the ≥35 cut-off point since it has been shown to be the most sensitive cut-off point for a probable diagnosis of post-traumatic stress (39). Moreover, we used this high cut-off point since patients with post-traumatic stress tend to overgeneralize their autobiographical thoughts (40, 41). When we lowered the cut-off point to ≥26, indicating clinical relevant symptoms of post-traumatic stress, post-traumatic stress rates in our trauma patients were more comparable to prevalence rates of post-traumatic stress as reported in previous studies (34-38).

A major strength of the BIOS study is the use of proxy assessments. As compared with participants who completed the questionnaires themselves, the group of participants who was represented by a proxy informant (n=407, 8% of the study population) included more females (50.6% and 73.5%, respectively) and more patients with low educational level (51.9% and 81.9%, respectively). Furthermore, differences were found between both groups regarding age (patient: median 67 years; IQR 49-81 years, proxy: median 85 years; IQR 80-90), hospital length of stay (patient: median 4 days; IQR 2-8, proxy: median 8 days; IQR 4-13 years), admission to an Intensive Care Unit (patient: 6.6%, proxy: 7.9% admissions) and injury severity as measured with the Injury Severity Score (patient: median 5; IQR 3-9, proxy: median 9; IQR 9-9). Most proxy informants (i.e. 64.1%) completed a BIOS questionnaire for a patient with a hip fracture. A previous study concluded that proxy responses are unlikely to be biased (42). In contrast, another study showed that proxy informants tend to overestimate baseline functioning when patient scores were low, whereas proxy informants tend to underestimate functioning when patient scores were high (43). Therefore, in *Chapter 5*, we excluded patients that were represented by a proxy informant when comparisons were made between HS prior to the trauma and HS of the general population. From a practical viewpoint, BIOS questionnaires were analysed as 'completed by a proxy informant' if more than half of the questionnaires were completed by a proxy participant. In 31 BIOS participants (0.63% of the total study population), questionnaires were alternately completed by a proxy informant and patients themselves. Nevertheless, the interchangeable use of proxy and patient responses should be analysed with great caution (42).

- *WHOQOL-BREF questionnaire*

A high percentage of missing items on the Abbreviated World Health Organization Quality of Life Instrument (WHOQOL-BREF) was found. A possible reason for this is that the WHOQOL-BREF questionnaire was added at the end of the already comprehensive set of BIOS questionnaires. Longer questionnaires are associated with higher rates of item non-response (44), leading to a loss of information.

Confounding

- *BIOS study*

We examined whether educational level could explain the difference in retrospectively self-reported HS prior to the trauma and the self-reported HS of a reference cohort. After adjustment for age, gender and educational level, the difference in pre-injury HS and the HS of the reference cohort increased, underlining that other variables also influence self-reported HS. Although recall bias (patients may remember their functioning prior to the trauma differently than it actually was (45)) and response shift (occurs when, aggravated by a life event such as a trauma, people do not maintain a consistent internal scale for their responses over time (46)) lead to a systematic overestimation of functioning prior to the trauma (47), residual confounding might have occurred in the results as presented in *Chapter 5*. Factors such as occupational status (48), living alone or not (48), activity level (49) or the presence of comorbidities (50-52) are presumed to also have a large influence on self-reported HS.

External validity

External validity refers to the ability to generalize study results to a more universal population (13). In this thesis, we aimed to expand the knowledge on the prevalence, recovery patterns and determinants of non-fatal outcome after trauma.

- *BIOS study*

We used data of all hospitals in the Dutch Noord-Brabant region and we made use of the Brabant Trauma Registry. The Noord-Brabant region has 2,4 million inhabitants and covers representative amounts of urban and rural populations (53). Results of the 1 week assessment might probably not be extrapolated, since results may have underestimated the adverse health effects. However, from the 1 month assessment onwards, results of the BIOS study may at least be generalized to the Dutch hospitalized trauma population and to comparable high-income countries. A wide range of determinants were included in the BIOS. However, we did not measure determinants that are also known to have a significant influence on non-fatal outcome, such as social support (54), complications (54, 55), type of treatment (56), coping (57) or self-efficacy (36, 57). Nevertheless, findings of a recent study conducted in the UK on self-reported HS and psychological outcome after trauma in patients aged 16-70 with the same study design (7, 58), resulted in comparable outcomes.

- *Systematic review*

The systematic review on the effect of SES on non-fatal outcome after trauma, included only peer-reviewed studies published in the English language. Besides, all 24 studies were performed in upper-middle or high-income countries (e.g. Australia or the USA). Therefore, it remained unknown whether the results of the systematic review may be extrapolated to lower-middle or low-income countries. Moreover, since the lack of a clear definition of SES, international standardization of SES is necessary.

- *Qualitative study*

The results of the qualitative study may not necessarily be extrapolated to trauma patients that are admitted to a Level 2 or Level 3 trauma center since we only included trauma patients that were admitted to a Level 1 trauma centre (providing the highest level of surgical care for trauma patients).

Conclusions and implications

In conclusion, this thesis showed that a trauma can have a large impact on patients' life. Improvements of self-reported HS over time were found during 2 years post-trauma in which most improvement in HS occurred within the first 3 months. However, the vast majority of the trauma patients had not fully recovered at 2 year post-trauma. Recovery patterns varied widely. In the long-term, patients at a higher age, with comorbidities, longer length of hospital stay, a lower extremity fracture or an injury of the spine showed lower self-reported HS. Besides, symptoms of posttraumatic stress were frequently reported. The qualitative study indicated that both physical, psychological, societal and environmental consequences can have a large influence on trauma patients' perceived QoL. Furthermore, this thesis provided further evidence for SES as an important determinant of non-fatal outcome after trauma. This thesis also revealed that the retrospectively assessed self-reported pre-injury HS of trauma patients was higher compared to the self-reported HS of a Dutch reference cohort. After adjustment for educational level, the difference in self-reported HS between both groups increased, underlining that other explanations are likely involved. Lastly, this thesis showed that the WHOQOL-BREF questionnaire can be used to validly and reliably assess QoL after trauma.

The findings of this thesis have both clinical and scientific implications as well as implications for policy makers.

Health care implications

Hospitalized trauma patients experienced substantial reductions in self-reported HS up until 2 years post-trauma. Besides, symptoms of posttraumatic stress were frequently self-reported. Results of the qualitative study in this thesis stress that health care providers have to inform patients and their relatives better about the consequences that may occur after trauma. Preferably at discharge, patients need to be better informed about the extent of recovery, the expected time of recovery as well as the psychological problems they may experience after trauma. Lastly, it is advised to inform patients on how to resume their live in practical ways (e.g. information regarding how to resume work) (59).

Health care providers should not solely focus on the physical consequences but they should be aware of all other possible consequences that may occur after trauma. To achieve this, a more holistic approach towards the treatment of trauma patients should be aimed in which patients' own perspective on their recovery should play a crucial role. Previous research found that the incorporation of patients' own perspective led to improvements in outcomes and led to more satisfaction with health care (60, 61).

Recognizing patients at an increased risk of worse outcome is a first step in optimizing trauma care. The WHOQOL-BREF questionnaire might be a useful tool in clinical practice since it may facilitate health care providers to detect unrecognized problems. Previous studies have already shown that the early recognition, treatment and monitoring of the physical and psychosocial consequences improve non-fatal outcome after trauma (7, 10, 58, 62, 63). Moreover, this thesis indicated that care coordination and the extension of the standard after care may be potentially useful techniques in the identification of trauma patients with a high risk of worse outcome.

Scientific implications

In line with a previous study (64), this thesis showed that the majority of patients does not recover completely up until 2 years after trauma. Also in line with the literature (65, 66), this thesis implied that other factors than the physical injury affect recovery. Therefore, there is a need for longitudinal follow-up studies beyond 2 years after trauma. Besides, more research is needed as well to examine the complex interaction between injury-related and sociodemographic determinants of non-fatal outcome after trauma.

- *BIOS study*

To produce valid estimates of the health impact and the decrease of functioning after trauma, information on patients' functioning prior to the trauma is crucial (67-70). In the BIOS, the retrospectively collected pre-injury EQ-5D-3L was used to interpret the change from HS prior to the trauma to post-trauma HS. However, recall bias and response shift may have led to an overestimation of the HS prior to the trauma.

More research is necessary to further explore the dissimilarities between the retrospectively collected self-reported pre-injury HS and the self-reported HS of the general population. For this, a more detailed insight into the differences between sociodemographic and health-related

characteristics between the trauma population and the general population is needed. Thereafter, the effects of these differences on self-reported HS should be examined in both populations.

Increasing response rates and minimizing the loss to FU are important areas for improvement in future prognostic cohort studies (71, 72). New approaches should be developed to replace the comprehensive sets of questionnaires that patients have to complete. One approach includes computerized adaptive testing (CAT) (73). Although CAT requires a high degree of technology, patient acceptance, extensive development of item pools and item calibration, it allows tailored-made short and precise domain-specific scales and it minimize floor and ceiling effects (73). In previous studies, CAT has already proven valid in other settings (73-76). Additionally, CAT improved response rates (77-79) and may even reduce loss to FU.

In order to increase comparability between studies, standardization of research is vital (47, 80, 81). Standardization of research methods will provide a more clear insight into the size of the trauma and the identification of risk groups. Moreover, standardization is necessary to set priorities for prevention and interventions. Future research should include all trauma causes, all types of trauma and all levels of injury severity. Subsequently, insight in the total burden of trauma will be obtained more accurately.

- *Systematic review*

Due to the absence of an explicit definition of SES it is difficult to determine the role of SES on non-fatal outcome after trauma. Therefore, research is necessary to more clearly define SES and requirements to accurately assess all relevant domains in the trauma setting. Because of the multidimensionality of SES, we recommend measuring multiple variables instead of a single variable to indicate SES.

- *Qualitative study*

This thesis revealed that patients' own expectations had a large influence on perceived QoL. Therefore, researchers should examine the role of trauma patient's own expectations regarding recovery. Future research should also focus on the psychosocial well-being of family members confronted with a trauma of their relative.

- *WHOQOL-BREF questionnaire*

The WHOQOL-BREF is a reliable and valid questionnaire for the assessment of QoL in the hospitalized trauma population. More research is necessary to further examine its psychometric properties, e.g. by testing the test-retest reliability.

Policy makers

The risk of becoming a trauma victim can be influenced by several sociodemographic characteristics, such as age (82). Elderly are at the highest risk of becoming a trauma victim. The mortality rate in elderly trauma patients is high (i.e. 15%) (83). When elderly do survive their trauma, this thesis revealed that self-reported HS is often seriously affected. In order to provide better non-fatal outcome after trauma in the elderly, an improved cooperation between health care systems and social services is desirable.

This thesis clearly indicated that a trauma has a large impact on patients and often has long-term consequences, resulting in a high disease burden. Prevalence and outcome data facilitate

the development of effective interventions. Psychological problems, including trauma-related psychological problems, have been neglected in public health (84). New strategies that improve psychological outcome after trauma should be introduced in order to further optimize non-fatal outcome after trauma, e.g. by screening patients on psychological problems.

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9

Chapter

Summary

Mortality rates in the trauma population have decreased over the past decades. Subsequently, it becomes increasingly important to examine non-fatal outcome. The aim of this thesis is to expand the knowledge on the prevalence, recovery patterns and determinants of non-fatal outcome after trauma for the hospitalized trauma population. This chapter provides a summary of the main findings of this thesis.

In *Chapter 2*, we described the research protocol of the Brabant Injury Outcome Surveillance (BIOS), a large prospective multicenter cohort study with 2 years of follow-up. The BIOS aimed to include adult trauma patients that are admitted to a hospital in the Dutch Noord-Brabant region in order to gain more insight into the prevalence, recovery patterns and predictors of functional and psychological outcome after non-fatal trauma. Data is collected by self-reported questionnaires or by telephone interviews at 1 week, 1, 3, 6, 12 and 24 months post-trauma. Results as presented in *Chapter 3,5* and *7* in this thesis are derived from the BIOS.

In *Chapter 3*, we examined the course of self-reported health status (HS) and the prevalence of self-reported psychological symptoms during the first 2 years after trauma in the 4,883 patients (50% response rate) participating in the BIOS. Shortly after trauma, a large decrease in HS was found. Most improvement in HS occurred within the first 3 months post-trauma. Self-reported HS at 2 year did not reach pre-injury levels or the Dutch general norm score. Self-reported symptoms of anxiety, depression or post-traumatic stress were reported in 10.2%, 12.3% and 13.5%, respectively, of the study population at 1 week post-trauma. The number of patients reporting symptoms of anxiety, depression or post-traumatic stress showed a minor decrease at 2 years post-trauma (to 7.8%, 6.8% and 11.0%, respectively). At long-term, patients at a higher age, with more comorbidities, longer length of hospital stay, a lower extremity fracture or an injury of the spine showed lower self-reported HS.

In *Chapter 4*, we conducted a systematic review to summarize the current knowledge of the effects of socio-economic status (SES) on non-fatal outcome after trauma. In addition, we critically examined the measurements and interpretations of SES. The studies included in the review showed large variations in methodological quality and the timing of follow-up measurements post-trauma ranged widely. To indicate SES, studies used a large number of variables in which educational level was used most frequently (alone or in combination with income). Although a multidimensional and valid measure of SES is lacking today, results showed that SES is an important determinant of non-fatal outcome after trauma since all studies found a positive association (80% statistically significant) between increased SES and better non-fatal outcome.

Previous literature has shown statistically significant differences between retrospectively collected self-reported HS prior to the trauma and self-reported HS of the general population. As compared with the general population, the trauma population includes a larger proportion of people with a low level of SES. SES is strongly associated with health. In *Chapter 5*, we examined whether educational level, as a measure of SES, could indeed explain the difference in outcomes between the retrospectively collected self-reported pre-injury HS and the self-reported HS of a Dutch reference cohort. For this purpose, we adjusted for age, gender and educational level. We found that the retrospectively assessed self-reported pre-injury HS was higher as compared with the self-reported HS of the reference cohort, even after adjustment

for age, gender and educational level. Most importantly, after correction for educational level, the difference in self-reported pre-injury HS and the self-reported HS of the reference cohort further increased, underlining that other explanations are likely involved.

In *Chapter 6*, we described the findings of a qualitative study which aimed to gain more insight into changes in perceived Quality of Life (QoL) after trauma. Four focus groups were conducted, in which the 20 participants who had had a trauma discussed and debated their experiences. The heterogeneous group of trauma patients, including a wide variety of age, types of trauma and injury severity, reported comparable consequences. In the first months post-trauma, physical limitations, independency, pain and anxiety predominated. Later, patients experienced problems with acceptance. The patients' feeling of the need to have control over their own situation, their own expectations and a social network were all related to QoL. As compared with the other patient groups, patients with traumatic brain injury (TBI) reported more psychosocial consequences and elderly reported more difficulties in performing (social) activities. In addition, this study showed that a trauma can also have a negative impact on partners' life, especially in TBI patients. Quality of health care was considered an important aspect in the patients' perceived QoL. Almost all patients stated that they received suboptimal aftercare. Overall, findings indicated that the impact of a trauma influences QoL in different health domains.

In *Chapter 7*, we examined the validity (i.e. the degree to which a questionnaire measures what it is supposed to measure) and reliability (i.e. measuring the accuracy of a measure) of the Abbreviated World Health Organization Quality of Life Instrument (WHOQOL-BREF) for the hospitalized trauma population. The WHOQOL-BREF questionnaire provides a detailed assessment of each individual facet that is related to QoL. Results of this study indicated that the WHOQOL-BREF had no problematic floor and ceiling effects and confirmatory factor analysis revealed a moderate model fit. The 26 items and the 4 domain scores showed nearly symmetrical distributions since mean scores were close to median scores, except for the *'general health'* item. The domains of the WHOQOL-BREF showed good internal consistency (i.e. the assessment of how reliably items that are designed to measure the same construct actually do so), except of the social domain. Taken together, the WHOQOL-BREF can be used to validly and reliable asses QoL in a heterogeneous group of hospitalized trauma patients.

In summary, this thesis indicates that a trauma has a large impact on patients' life including long-lasting consequences.

10

Chapter

Summary in Dutch

Wereldwijd vormen ongevallen, ook wel trauma's genoemd, een groot probleem voor de volksgezondheid. De toedracht van een trauma kan heel divers zijn, zoals een verkeersongeval, verdrinking, valpartij of een geweldsincident. Een trauma kan variëren van een lichte verwonding in één lichaamsregio tot meerdere ernstige verwondingen in verschillende lichaamsregio's. Daarnaast kent de traumapopulatie een grote verscheidenheid in sociodemografische kenmerken, zoals leeftijd, geslacht en opleidingsniveau. Jaarlijks worden er in Nederland ruim 80.000 traumapatiënten in een ziekenhuis opgenomen. De medische en ziekteverzuimkosten van deze patiënten bedragen jaarlijks 3,5 miljard euro.

In de afgelopen decennia is er een sterke daling zichtbaar geweest in het sterftecijfer van traumapatiënten. In Nederland komt ca. 2% van alle opgenomen traumapatiënten te overlijden, 98% van de patiënten overleeft dus het trauma. Een deel van deze patiënten krijgt te maken met fysieke en/of psychologische problemen ten gevolge van het trauma, die blijvend van aard kunnen zijn. In dit proefschrift worden de prevalentie, herstelpatronen en risicofactoren van niet-fatale uitkomsten na een trauma onderzocht.

In *Hoofdstuk 2* beschrijven we het onderzoeksprotocol van de Brabant Injury Outcome Surveillance (BIOS), een grote cohortstudie naar niet-fatale uitkomsten na een trauma. Aan de BIOS studie doen volwassen traumapatiënten mee die opgenomen zijn in één van de Noord-Brabantse ziekenhuizen. In de BIOS studie is onderzocht hoe het herstel na een trauma verloopt en welke patiënten een verhoogd risico hebben op een verminderd functioneren na een trauma. Gegevens zijn verzameld 1 week, 1, 3, 6, 12 en 24 maanden na het trauma door middel van zelfgerapporteerde vragenlijsten en telefonische interviews.

In *Hoofdstuk 3* hebben we de zelfgerapporteerde gezondheidstoestand bij traumapatiënten onderzocht. Daarnaast bestudeerden we hoe vaak symptomen van een angststoornis, depressie of posttraumatische stress na een trauma voorkwamen. Ook identificeerden we patiëntgroepen met een verhoogd risico op een verminderde gezondheidstoestand na een trauma. Dit is onderzocht bij de 4,883 deelnemers aan de BIOS studie. Kort na het trauma was er een grote afname te zien in de gezondheidsstatus van de deelnemers. De grootste verbetering van de zelfgerapporteerde gezondheidstoestand trad op in de eerste 3 maanden na het trauma. Twee jaar na het trauma rapporteerden patiënten gemiddeld gezien een lagere gezondheidstoestand dan vóór het trauma. Een deel van de patiënten rapporteerde symptomen van een angststoornis, depressie of posttraumatische stress (respectievelijk 10.2%, 12.3% en 13.5% 1 week na het trauma). Deze psychologische symptomen lieten slechts een geringe afname zien naarmate de tijd verstreek: 2 jaar na het trauma had respectievelijk 7.8%, 6.8% en 11.0% last van symptomen van een angststoornis, depressie of posttraumatische stress. In de BIOS studie bleken de volgende factoren een risicofactor te zijn voor een lagere zelfgerapporteerde gezondheidstoestand na het trauma: hogere leeftijd, aanwezigheid van één of meerdere gezondheidsaandoeningen voorafgaand aan het trauma (zoals hart- en vaatziekten), langere ziekenhuisopname, een botbreuk in het bekken/been of een letsel van de wervelkolom/dwarslaesie.

In *Hoofdstuk 4* hebben we een systematisch literatuuronderzoek uitgevoerd om de effecten van sociaaleconomische status (SES) op niet-fatale uitkomsten na een trauma samen te vatten. SES kan op verschillende manieren gemeten worden, bijvoorbeeld aan de hand van opleidingsniveau of inkomen. Om die reden hebben we de SES-indicatoren van de 24 studies

die werden meegenomen in dit onderzoek, kritisch bekeken. De studies toonden een grote variëteit in methodologische kwaliteit. Een voorbeeld hiervan was de grote verscheidenheid in uitvoering en rapportage van de statistische analyses. Daarnaast liepen de meetmomenten van de studies sterk uiteen, variërend van vrijwel direct na het trauma tot 6 jaar na het trauma. Opleidingsniveau werd het vaakst gebruikt als graadmeter voor SES (alleen of in combinatie met inkomen). Alle studies vonden een positief verband (80% statistisch significant) tussen een hogere SES en beter functioneren na een trauma. Hoewel er momenteel geen adequate, uniforme en multidimensionale maat voor SES bestaat, tonen de resultaten van dit literatuuronderzoek aan dat SES een grote invloed heeft op niet-fatale uitkomsten na een trauma.

Eerdere onderzoeken tonen aan dat er aanzienlijke verschillen bestaan tussen de retrospectief (met terugwerkende kracht) verzamelde zelfgerapporteerde gezondheidstoestand van patiënten voorafgaand aan het trauma en de zelfgerapporteerde gezondheidstoestand van de algemene bevolking. In verhouding tot de algemene bevolking heeft de traumapopulatie een groter aandeel personen met een lage SES. SES is sterk gerelateerd aan de gezondheidstoestand. In *Hoofdstuk 5* onderzochten we of opleidingsniveau, als maat voor SES, daadwerkelijk het verschil in uitkomsten tussen de retrospectief verzamelde zelfgerapporteerde gezondheidstoestand voorafgaand aan het trauma en de zelfgerapporteerde gezondheidstoestand van de algemene bevolking kan verklaren. Omdat de traumapopulatie en de algemene bevolking verschillen op enkele belangrijke sociodemografische kenmerken, zoals leeftijd, geslacht en opleidingsniveau, corrigeerden we hiervoor in de statische analyses. Resultaten wijzen erop dat er naast leeftijd, geslacht en opleidingsniveau andere factoren zijn die mogelijk een rol spelen met betrekking tot de verschillen in de zelfgerapporteerde gezondheidstoestand van de traumapopulatie voorafgaand hun trauma en die van de algemene bevolking.

In *Hoofdstuk 6* onderzochten we welke Kwaliteit van Leven (KvL) veranderingen er na een trauma worden ervaren. Vier focusgroepen vonden plaats, waarbij 20 deelnemers die allen een trauma hadden gehad hun persoonlijke ervaringen bespraken en bediscussieerden. Ondanks de grote variatie in leeftijd, soort en ernst van het trauma, rapporteerden de patiënten vrijwel identieke gevolgen. In de eerste maanden na het trauma overheersten fysieke beperkingen, pijn en angst. Patiënten wilden het liefst zoveel mogelijk onafhankelijk zijn van anderen. Later ondervonden patiënten problemen met de acceptatie van de blijvende gevolgen van het trauma. Het gevoel dat patiënten controle over hun eigen situatie hadden, hun eigen verwachtingen ten aanzien van het herstel en het hebben van een sociaal netwerk waren allen gerelateerd aan KvL. Daarnaast toont deze studie aan dat een trauma ook een negatief effect kan hebben op het leven van partners van traumapatiënten. Dit geldt met name bij partners van patiënten met traumatisch hersenletsel. De ervaren kwaliteit van de gezondheidszorg werd als een belangrijk aspect beschouwd in de ervaren KvL. Vrijwel alle deelnemers gaven echter aan dat nazorg voor traumapatiënten verbeterd moet worden. Samenvattend toont deze studie aan dat een trauma een grote impact kan hebben op de ervaren KvL.

In *Hoofdstuk 7* onderzochten we de validiteit (toont aan of een meetinstrument meet wat het zou moeten meten) en betrouwbaarheid (meet de nauwkeurigheid en precisie van een meetprocedure) van de verkorte versie van de Wereldgezondheidszorgorganisatie Kwaliteit van Leven vragenlijst (*Engels: Abbreviated World Health Organization Quality of Life, WHOQOL-BREF*) vragenlijst. De WHOQOL-BREF meet alle facetten die KvL omvat. Met uitzondering van het sociale domein, vertoonden de domeinen van de WHOQOL-BREF een goede interne consistentie (geeft aan

in hoeverre verschillende items van een vragenlijst die eenzelfde kenmerk beogen te meten, dat ook daadwerkelijk doen). Dit onderzoek toont aan dat de WHOQOL-BREF een valide en betrouwbare vragenlijst is om de KvL te meten bij traumapatiënten.

Implicaties en aanbevelingen

Met dit proefschrift tonen we aan dat een trauma een grote impact kan hebben op het leven van patiënten. Onze resultaten hebben implicaties voor zorgverleners en patiënten, onderzoekers en beleidsmedewerkers. Daarnaast geven we op basis van de resultaten van dit proefschrift enkele aanbevelingen om de niet-fatale uitkomsten na een trauma verder te verbeteren.

Zorgverleners en patiënten

- We raden zorgverleners aan om hun patiënten en diens familieleden beter te informeren over de mogelijke gevolgen van een trauma. Bij ontslag uit het ziekenhuis is het wenselijk patiënten beter te informeren over de mate van het herstel, de verwachte hersteltijd en de psychologische problemen die zich voor kunnen doen.
- De WHOQOL-BREF vragenlijst kan een goed hulpmiddel zijn in de klinische praktijk om het herstel van patiënten over de tijd te volgen en om mogelijke factoren die samenhangen met een verminderd herstel, op te sporen.
- Zorgcoördinatie (bijvoorbeeld door het aanstellen van een casemanager) en de uitbreiding van de standaard nazorg zijn mogelijk effectieve middelen om patiënten met een verhoogd risico op een lagere gezondheidstoestand na een trauma beter te kunnen identificeren en te begeleiden.

Wetenschappelijk onderzoek

- Om de daadwerkelijke impact van een trauma te onderzoeken, is informatie over het functioneren van de patiënt voorafgaand aan het trauma cruciaal. Onderzoeken naar niet-fatale uitkomsten na een trauma zouden om die reden informatie moeten verzamelen over het functioneren van de patiënt vóór het trauma. In de BIOS studie was de retrospectief verzamelde zelfgerapporteerde gezondheidstoestand voorafgaand aan het trauma namelijk van groot belang bij de interpretatie van de verandering in de gezondheidstoestand na het trauma.
- Het verhogen van het percentage deelnemers aan een studie en het verminderen van vroegtijdige uitval gedurende de looptijd van een studie zijn belangrijke punten van verbetering voor toekomstige studies. Er zal gebruik gemaakt moeten worden van innovatieve oplossingen om het aantal vragen te reduceren zonder informatie te verliezen. Een voorbeeld van zo'n nieuwe methode is computer adaptief testen.
- Er zijn uiteenlopende onderzoeksmethoden om niet-fatale uitkomsten na een trauma te meten. Om de vergelijkbaarheid tussen studies te vergroten is standaardisatie van studiepopulaties, meetmomenten en de keuze van vragenlijsten noodzakelijk. Deze standaardisatie zal ervoor zorgen dat resultaten van verschillende studies samengevoegd kunnen worden. Hierdoor zal er een beter inzicht verkregen worden in de gevolgen van een trauma evenals de identificatie van patiëntgroepen met een verhoogd risico op een slechtere uitkomst.
- Aangezien er geen eenduidige manier is om SES te meten, is het moeilijk om het daadwerkelijke effect van SES op niet-fatale uitkomsten na een trauma te onderzoeken. Daarom is er onderzoek nodig om SES duidelijker te definiëren. Omdat SES een multidimensionaal begrip is, raden we onderzoekers aan om SES te definiëren aan de hand van meerdere variabelen.

- Het is wenselijk meer onderzoek te doen naar de rol van de eigen verwachtingen van traumapatiënten ten aanzien van hun herstel. Ook is het raadzaam om het psychosociale welzijn van familieleden die worden geconfronteerd met een trauma van hun familielid, te bestuderen.
- Aanvullend onderzoek is nodig om de psychometrische eigenschappen van de WHOQOL-BREF vragenlijst nog gedetailleerder in kaart te brengen. Een voorbeeld hiervan is het onderzoeken van de test-hertest betrouwbaarheid van de WHOQOL-BREF.

Beleidsmedewerkers

- Verschillende sociodemografische factoren, zoals leeftijd, worden geassocieerd met een verhoogd risico om slachtoffer te worden van een trauma. Ouderen hebben een sterk verhoogd risico op een trauma. Het aandeel oudere patiënten dat komt te overlijden als gevolg van een trauma is hoog (15%). Wanneer ouderen het trauma overleven, laat dit proefschrift zien dat dit vaak grote gevolgen heeft voor hun gezondheidstoestand. Om de niet-fatale uitkomsten na een trauma bij ouderen verder te verbeteren, is een nauwe samenwerking tussen gezondheidsdiensten en sociale diensten wenselijk.
- Zelfgerapporteerde symptomen van angst, depressie of posttraumatische stress worden gerelateerd aan een slechtere gezondheidstoestand na een trauma. Om de gevolgen na een trauma verder te reduceren, zullen beleidsmedewekers meer aandacht moeten besteden aan de erkenning en behandeling van psychologische problemen na een trauma.

11

Chapter

List of publications
Acknowledgements
Curriculum Vitae
PhD portfolio

LIST OF PUBLICATIONS

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Kruithof N, Polinder S, de Munter L, van de Ree C.L.P, Lansink K.W.W, de Jongh M.A.C, BIOS-group. Health status and psychological outcome after trauma; a prospective multicenter cohort study. *Submitted.*

ACKNOWLEDGEMENTS

Vanzelfsprekend heb ik dit onderzoek niet alleen uitgevoerd. Graag wil ik dan ook iedereen bedanken die dit onderzoek voor mij mogelijk heeft gemaakt. Een aantal personen wil ik in het bijzonder bedanken.

Suzanne en Mariska, bedankt voor de prettige samenwerking de afgelopen jaren. Suzanne, ik heb je manier van begeleiden als bijzonder prettig ervaren. Je bent een enorm gedreven onderzoeker. Je gaf op een hele prettige manier feedback op stukken waarbij het vaak leek alsof je mijn gedachten kon lezen. Mariska, zeker in het eerste jaar van mijn promotie heb je heel veel voor me betekend. Het opzetten van de BIOS bleek moeilijker dan in eerste instantie gedacht. Dank dat je me hierin goed hebt begeleid, maar dat je me ook mijn eigen gang liet gaan. Tijdens mijn promotieonderzoek heb ik heel veel van jullie geleerd.

Prof. dr. Jan Anne Roukema, ik was een promovendus 'op afstand', onder de hoede van Suzanne en Mariska. De overleggen waren altijd gezellig en er werd, na een korte update over de stand van zaken en de mogelijke implementatie van mijn onderzoek, gesproken over vanalles en nog wat. Dank voor deze gesprekken.

Ik bedank alle traumachirurgen die betrokken zijn geweest bij de opzet en uitvoering van de BIOS: Percy van Eerten, dr. Floortje van Eijck, dr. Erwin van Geffen, Wilbert Haagh, Lodewijk Poelhekke, Jan Bernard Sintenie, Charles Stevens, dr. Alexander van der Veen, dr. Cees van der Vlies en dr. Dagmar Vos.

Daarnaast wil ik de volgende personen bedanken die hun bijdrage hebben geleverd bij de uitvoering van de BIOS: Wilma van Riel, Theo Harte en Thea Hofland van de backoffice SEH van het Elisabeth-TweeSteden ziekenhuis, locatie Elisabeth; de SEH-baliemedewerkers van het Elisabeth-TweeSteden ziekenhuis, locatie Twee-Steden; Stacey Mans, Mark van den Baar en de SEH-verpleegkundigen van het Máxima Medisch Centrum; de SEH-secretaresses en baliemedewerkers van het Bravis ziekenhuis; Theo Lanhoij, Pierre van Erven, artsen en arts-assistenten van het St. Anna Ziekenhuis; de SEH-verpleegkundigen, in het bijzonder Franca Robben, van het Maasziekenhuis Pantein; de SEH-secretaresses van het Elkerliek ziekenhuis; dr. Paul Johannesma en de SEH-secretaresses van het Jeroen Bosch Ziekenhuis; Claudia Verhoeven en Imke Maas van ziekenhuis Bernhoven; de artsen en arts-assistenten, in het bijzonder Lotje Emmen en Jeroen Bransen, van de SEH van het Catharina ziekenhuis; dr. Margriet van Baar van het Maasstad ziekenhuis; en Jacqueline Oomen en de SEH-verpleegkundigen van het Amphia ziekenhuis.

Ik wil ook alle deelnemers bedanken voor de tijd die zij in dit onderzoek hebben gestoken. Ik wil de patiënten en partners die deelnamen aan de focusgroepen bedanken voor hun openhartigheid en ik dank de duizenden patiënten en familieleden/naasten die de vragenlijsten van de BIOS-studie keer op keer hebben ingevuld.

Ook wil ik alle stagiaires bedanken: Kari Ploegsma, Bonnie Biesbroeck, Anne de Krijger, Elise van der Sluijs, Inge van Alst, Carmen van Meer, Ellen Kemps, Wart Bagijn, Nikki van Beeck, Matthijs van Peperstraten, Nigel Drunen, Nicole Gordon, Mara van den Assem, Thijs van der Putten, Ties van Gemert, Dagmara Bloch, Anne Leurs, Rosa Maas, Ilse van de Wiel, Ralf van Delden, Sarah Wakker, Mirte van Leeuwen, Elise Immink, Melissa de Waal, Tommy Broeders, Linda Brauwer, Chantal Brinksma, Meraud van Casteren, Jonne Verschure, Christianne Spohr, Amalia Musters, Noa Zoetmulder, Irem Balkaya, Charlotte van den Heuvel, Jasmijn Liedtke, Nicky Vervloet, Cyntha Minderhoud, Inge Nijman, Jeroen Lutterman, Eda Canikli, Celine Smets, Avya Axwijk, Lieke Meulemans, Ruben Amantuni, Loes van de Ven en Inge van Erp. Alyssa Venema, Esmee Lepelaars, Mandy Jeekel, Nele van Bedaf, Koen Pey en Carlijn van Sambeek, Jeanette Schräder, Els Boender, Marien Diemel en Christine Hagendooren, ook ontzettend bedankt voor jullie inzet. Yvette Hermans, bedankt voor de secretariële ondersteuning. Zonder jullie was de uitvoering van de BIOS-studie vrijwel onmogelijk geweest. Bedankt voor het vele werk dat jullie hebben gedaan en daarmee jullie bijdrage aan dit proefschrift.

Beste co-auteurs, bedankt voor jullie bijdrage. Prof. dr. Jolanda de Vries en dr. Marjan Traa, ik wil jullie bedanken voor jullie hulp en kritische blik bij het uitvoeren en uitwerken van het kwalitatieve onderdeel van mijn proefschrift. Marjan, bedankt dat jij me het vertrouwen gaf om de focusgroepen te leiden. Maria Karabatzakis, dank dat ik altijd op je kon rekenen bij het analyseren en interpreteren van de resultaten van de de focusgroep- en de validatiestudie. Dr. Juanita Haagsma, bedankt voor de prettige samenwerking en je motiverende feedback. Dr. Maryse Cnossen, bedankt dat je het 'laatste puzzelstukje' hielp toe te voegen aan de validatiestudie.

Koen Lansink, het was fijn om jouw frisse blik op het onderzoek te horen als we helemaal diep in het onderzoek verzonken zaten. Lars Brouwers, bedankt voor je bijdrage aan de BIOS. Ik heb zelden iemand ontmoet die zo bevlogen in zijn werkzaamheden is.

Ik wil al mijn Kamer 7-collega's heel erg bedanken: Maureen Tan, Leonie de Munter, Marc van de Ree, Hugo Aben, Marleen van Eyck, Eva Visser, Stefan Hartveldt, Maria Karabatzakis, Johan Telleman, Wouter Bakker en Claudia Raaijmakers. Maureen, Leonie en Marc, we hebben de afgelopen jaren veel samengewerkt. Maureen en Leonie, zonder jullie deskundigheid en scherp inzicht in de wirwar van BIOS-data, had dit proefschrift er niet in deze vorm gelegen. Bedankt daarvoor! Leonie en Marc, we hebben in de afgelopen jaren veel met elkaar kunnen sparren over onderzoeksmethoden en statistiek. Marc, in de beginperiode hebben we veel samengewerkt om de BIOS in alle ziekenhuizen te laten draaien. Je leerde me het reilen en zeilen van het ziekenhuis, bedankt hiervoor. Leonie, bedankt voor je kritische blik en advies. Ik bewonder je manier van werken. Jullie hebben voor mij altijd een hele goede werksfeer gecreëerd. Met veel plezier denk ik terug aan de congresbezoeken en de gezamenlijke etentjes met jullie. Bedankt voor deze mooie tijd!

Daarnaast wil ik al mijn vrienden bedanken, in het bijzonder Mieke. Mieke, sinds we elkaar hebben leren kennen op de middelbare school hebben we samen heel wat kilometers wandelend (al dan niet met blaren), fietsend of hardlopend afgelegd. Dank dat ik altijd bij je terecht kan als dat nodig is.

Lieve mama en papa, dank jullie voor jullie onvoorwaardelijke liefde, steun en vertrouwen in mij. Jullie hebben het altijd voor mij mogelijk gemaakt om mijn hart te volgen. Mijn broers en zussen wil ik ook bedanken voor hun getoonde interesse de afgelopen jaren. Loesje, je laat me zien dat hele gewone dingen heel bijzonder zijn. Jullie betekenen heel veel voor me!

Remy, iech haw vaan diech. Op euze touwkoms same!

Nena Kruithof

CURRICULUM VITAE

Nena Kruithof was born on December 3, 1990 in Woerden, the Netherlands. In 2009, she completed her pre-university education (Algemeen Secundair Onderwijs, Latijn-wetenschappen) at College Heilig Kruis St. Ursula, Maaseik, Belgium. In 2012 she completed the shortened 3-year Bachelor in Physical Therapy at Zuyd University of Applied Sciences in Heerlen, in cooperation with Maastricht University. In 2014, she obtained her Master of Science degree in Biology of Human Performance and Health at Maastricht University. From 2012 to 2015, Nena worked at Fysiotherapie van de Schoor–de Maat as an allround physical therapists and she was involved in the implementation of a tailored quality system. From 2014 to 2015, she also worked as a researcher at the Research Center for Autonomy and Participation of people with a chronic illness at Zuyd University of Applied Sciences. In 2015 she started her PhD research focussing on non-fatal outcome after trauma at the Elisabeth-TweeSteden Hospital in Tilburg, which resulted in this thesis. Currently, Nena is working as a physical therapist, as a researcher at the Centre of Expertise for Innovative Care and Technology (EIZT) and as a lecturer at the Physical Therapy department of Zuyd University of Applied Sciences.

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PHD PORTFOLIO

Presentations at national and international conferences

Elisabeth-Twee Steden Hospital, Trauma TopCare symposium, Tilburg, the Netherlands (poster)	2016
Elisabeth-Twee Steden Hospital, Research symposium (poster)	2016
International Society for Quality of Life Research, Copenhagen, Denmark (poster)	2016
European Society for Trauma and Emergency Surgery, Bucharest, Romania	2017
Elisabeth-Twee Steden Hospital, Trauma TopCare symposium, Tilburg, the Netherlands	2017
Elisabeth-Twee Steden Hospital, Research symposium, Tilburg, the Netherlands (poster)	2017
Dutch Congress of Rehabilitation Medicine, Maastricht, the Netherlands (poster, nominated for best student poster award)	2017
Dag van de fysiotherapeut, Barneveld, the Netherlands (poster)	2017
Nationale traumadagen, Amsterdam, the Netherlands (poster)	2017
Nationale chirurgendagen, Veldhoven, the Netherlands	2018
International Society of Physical and Rehabilitation Medicine, Paris, France (poster)	2018
International Society for Quality of Life Research, Dublin, Ireland (poster)	2018
Dutch Congress of Rehabilitation Medicine, Groningen, the Netherlands (poster, nominated for best poster)	2018
World Confederation for Physical Therapy congress, Geneva, Switzerland (poster)	2019

Courses

Good Clinical Practice, Tilburg, the Netherlands	2015
Systematic Review and Meta-analysis, Tilburg University, Tilburg, the Netherlands	2015
Ethics in Social Sciences, Tilburg University, Tilburg, the Netherlands	2015
Constructing and Analyzing questionnaires, Tilburg University, Tilburg, the Netherlands	2016
Scientific writing in English for publication in Biomedical Journals, Text and training, Tilburg, the Netherlands	2016
Practical Biostatistics part II: multiple linear regression, logistic regression, repeated measurements (e-learning), Academisch Medisch Centrum, Amsterdam, the Netherlands	2017
Using R for statistics in Medical Research, Erasmus MC, Netherlands Institute for Health Sciences, Rotterdam, the Netherlands	2018
Repeated Measurements, Erasmus MC, Netherlands Institute for Health Sciences, Rotterdam, the Netherlands	2018

Workshops

Academic Visualization, Tilburg University, Tilburg, the Netherlands	2016
Writing grant proposals/introduction to funding opportunities after your PhD, Tilburg University, Tilburg, the Netherlands	2016
The use of Patient Reported Outcome Measures (PROMs) in healthcare, Zorginstituut Nederland, Nijmegen, the Netherlands	2017
Implementation of Medical Health Research, ZonMW, Den Haag, the Netherlands	2018